SYMPOSIUM ON ANESTHESIA NUMBER

Vol. 18 JULY, 1945 No. 1

SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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CONTENTS

Original Communications

Symposium on Anesthesia

Factors Influencing Trends in Anesthesia. John S. Lundy, M.D., R. Charles Adams, M.D., and Thomas H. Seldon, M.D., Rochester, Minn. ---- 1
Explosions in Anesthesia. Frank Cole, M.D., Minneapolis, Minn. ---- 7
Cyclopropane—A Personal Evaluation. Ralph M. Waters, M.D., Madison, Wis. ---- 26
Prolonged Anesthesia. Ralph T. Knight, M.D., and Joe W. Baird, M.D., Minneapolis, Minn. ---- 33
Intercostal Nerve Block. Stanton Belinkoff, M.D., New York, N. Y. ---- 37
Notes Regarding the Use of Intravenous Sodium Pentothal Anesthesia in Major Surgical Cases. Cleveland H. Shutt, M.D., St. Louis, Mo. ---- 43
Curare in Anesthesia. Stuart C. Cullen, M.D., Iowa City, Iowa ---- 45
Anesthetic Agents as Factors in Circulatory Reactions Induced by Hemorrhage. B. W. Zweifach, Ph.D., S. G. Hershey, M.D., E. A. Rovenstine, M.D., R. E. Lee, Ph.D., and R. Chambers, Ph.D., New York, N. Y. ---- 48

Pulsion Diverticulum of the Hypopharnyx at the Pharyngo-Esophageal Junction. Stuart W. Harrington, M.D., Rochester, Minn. ---- 66
Closure of the Bronchial Stump Following Lobectomy or Pneumonectomy. Richard H. Sweet, M.D., Boston, Mass. ---- 82
Ligation of the Inferior Vena Cava. Robert O. Northway, M.D., and Robert W. Buxton, M.D., Ann Arbor, Mich. ---- 85
Osteomyelitis of the Skull—Its Treatment With Penicillin and Repair of the Defect With Tantalum. Major Max T. Schnitker, Medical Corps, and Captain William D. McCarthy, Dental Corps, Army of the United States ---- 94
Radical Duodenopancreatectomy. J. E. Strode, M.D., F.A.C.S., Honolulu, Hawaii ---- 115

Editorial

Anesthesia. Ralph T. Knight, M.D., Minneapolis, Minn. ---- 130

Book Reviews

Book Reviews ---- 131

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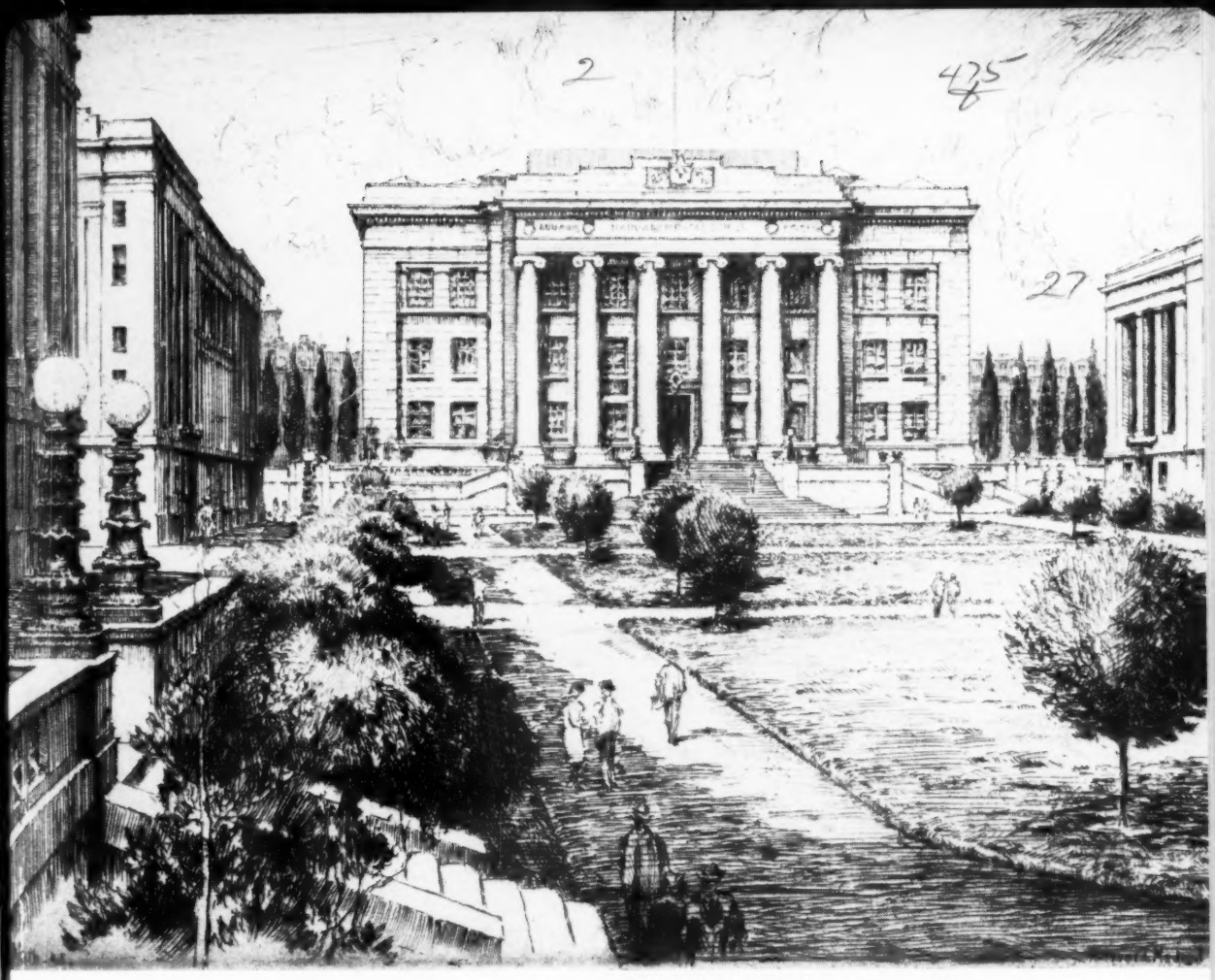


FROM AN ORIGINAL ETCHING BY ERNEST D. ROTH, N. A.

THE HARVARD SCHOOL OF MEDICINE was started as a branch of the University at Cambridge, Massachusetts, in 1782 and moved to Boston in 1810 to be near the growing hospital facilities of the city. Today the modern buildings of the Harvard School of Medicine are surrounded by some of Boston's largest and finest hospitals, which offer almost unlimited opportunities for clinical teaching and investigation. Many distinguished surgeons and physicians were graduated from this famous school.

Experience is the foundation on which all successful careers in the surgical and medical world are built. It is also the basis on which progress is made in the production and improvement of surgical sutures. D&G has gained long and valuable experience through its thirty-seven years of specialization in this field, and as a result has been able to make many important advances in suture quality. D&G research and product development are constantly contributing to new and finer techniques in surgery. Illustrated and described on the following pages are a few phases of D&G's broad service in sutures.

Incisions that Minimize Wound Disruption

AN IMPORTANT ADVANCE IN THE TECHNIC OF SUTURING

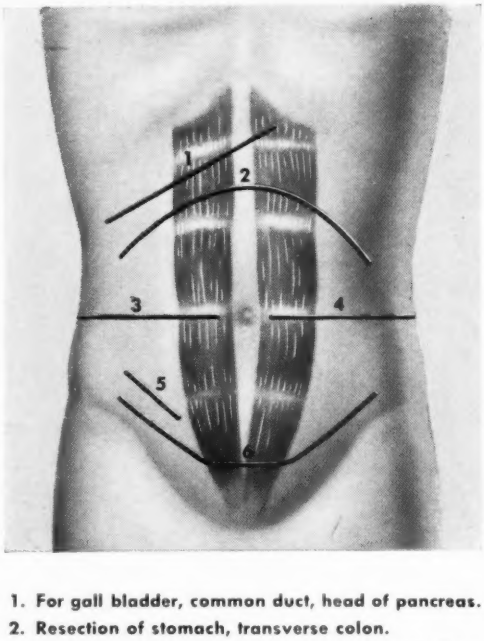
The employment of operative incisions which offer maximal assurance against sutures pulling through the tissues eliminates one of the principal causes of wound disruption and lessens the possibility of post-operative herniation.

Sutures hold most securely if the connective tissues within the wound are approximated in such a manner that the sutures must pull against the fibres within these layers. This necessitates cutting the connective tissues parallel to the direction of their fibres which, in the anterior abdominal wall, is usually best accomplished through a transverse initial skin incision.

In the past, transverse abdominal incisions have not found wide acceptance because they necessitate cutting across muscles in which sutures hold poorly and almost invariably cause tissue necrosis.

In the new technic of suturing transverse incisions, no attempt is made to suture muscle —only the surrounding sheath. Approximation of the muscle edges is further aided by keeping the patient in a semi-reclining position with knees partially flexed.

Because of the favorable results attending increasing use of this technic, and the current interest in principles which may facilitate early ambulation, D&G presents a series illustrating the incisions, and methods of suturing them.



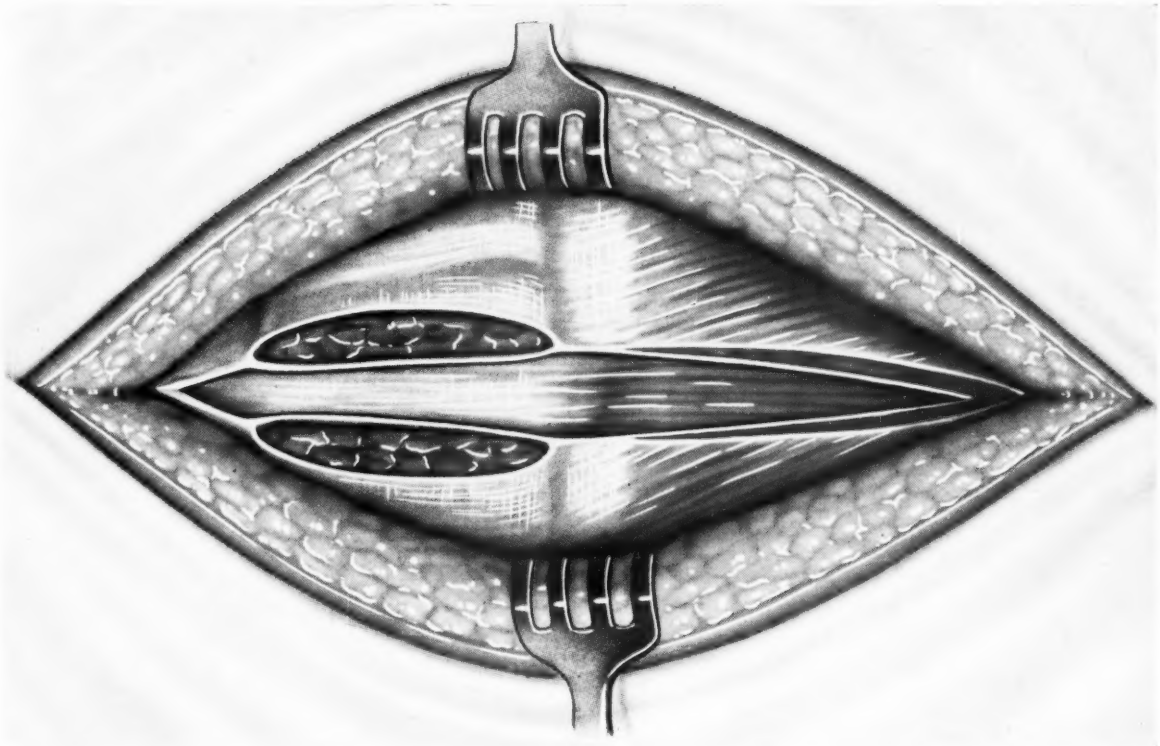
1. For gall bladder, common duct, head of pancreas.
2. Resection of stomach, transverse colon.
*3. Resection of ascending colon, cecum, right sided lesions.
*4. Descending colon, spleen and left sided lesions.
5. Appendectomy.
6. Pelvic surgery, resection of sigmoid.

NUMBERS THREE AND FOUR OF A SERIES

*RESECTION OF ASCENDING AND DESCENDING COLON

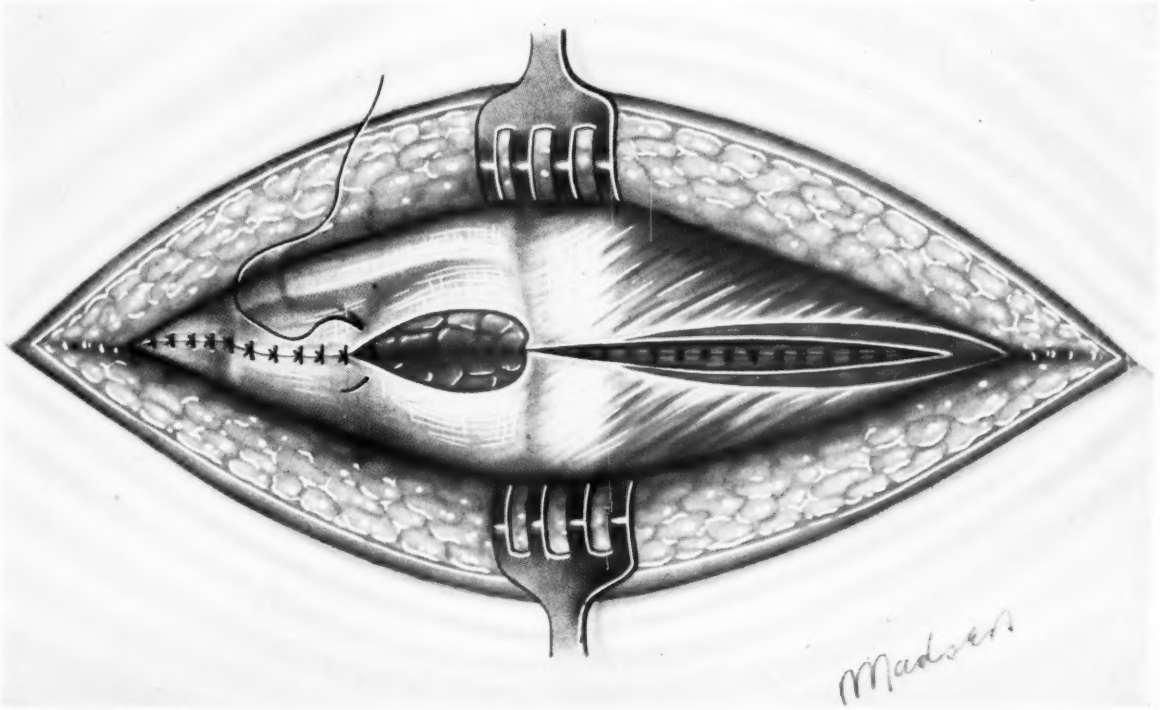
The incision shown (4) is being made on the left exposing the descending colon and sigmoid. To expose the cecum and ascending colon a similar incision (3) can be made on the right.

The skin incision extends from the linea alba to the angle between the ribs and the crest of the ilium. After the subcutaneous fat is cut the anterior rectus sheath is split in the direction of its fibres. The rectus muscle is divided at right angles. Two or three large bleeders must be clamped and ligated within the muscle. The inferior epigastric vessels are divided between clamps and ligated. The posterior sheath and peritoneum are cut in the direction of the fibres of the sheath. The entrance into the peritoneal cavity is usually made toward the midline and then the incision is extended laterally into the internal oblique. An excellent exposure of the lumbar gutter is obtained, particularly if the patient is tilted toward the opposite side.



The peritoneum and posterior sheath are approximated first with interrupted sutures. The rectus muscles are not sutured, although the fasciae of the internal oblique are caught in the suturing of the posterior and anterior sheaths. The anterior sheath is closed with interrupted sutures. The sutures pull against the fibres of both the anterior and posterior sheaths giving strength to the wound. The skin is closed in the usual manner.

When required, a drain is brought out at the lateral angle of the wound.



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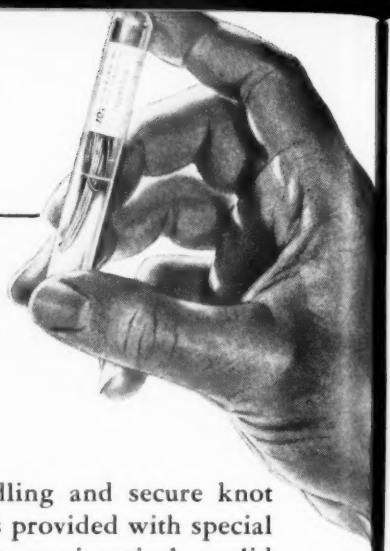

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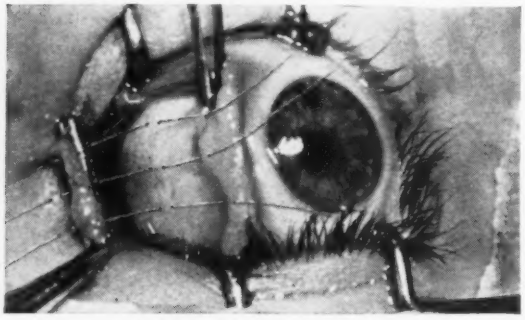
The wide range of suture needle combinations which D&G has developed and made available has aided the progress of ophthalmic surgery by extending to this field the atraumatic principle which among other advantages reduces trauma to an absolute minimum.



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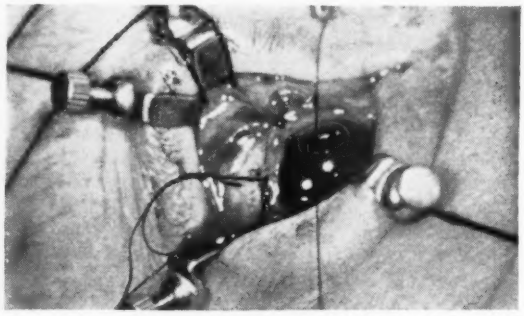

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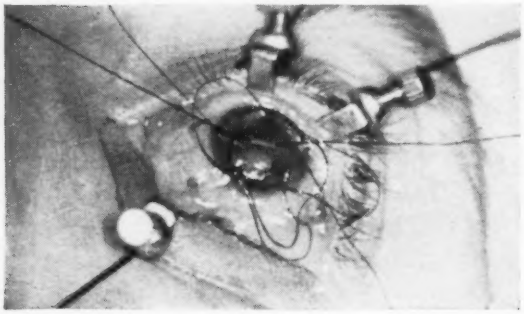

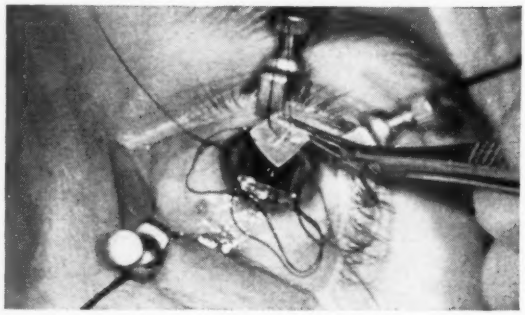

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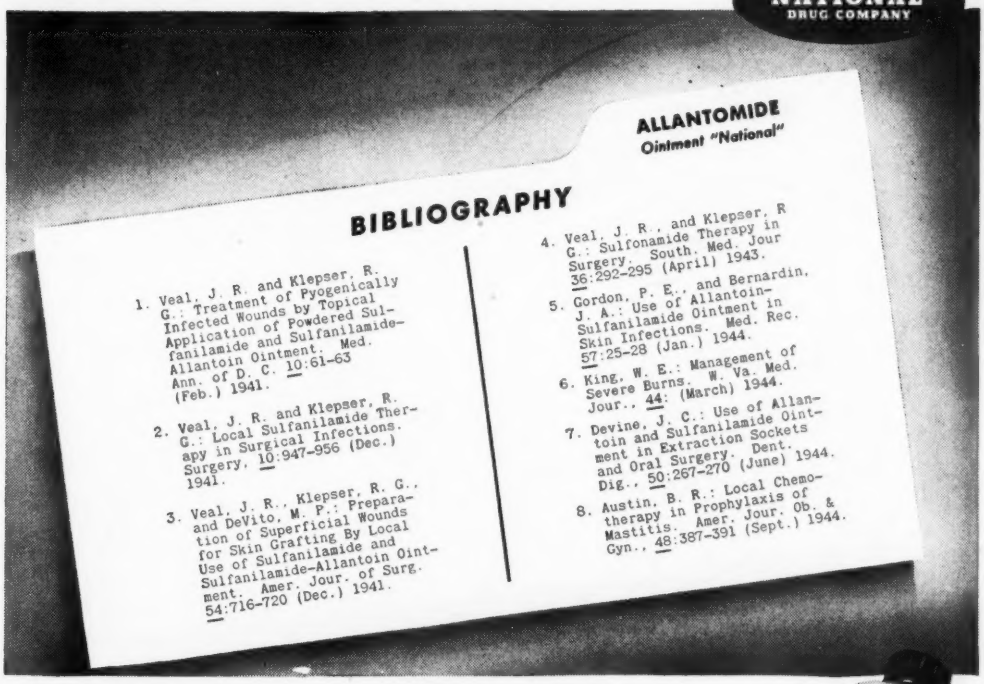
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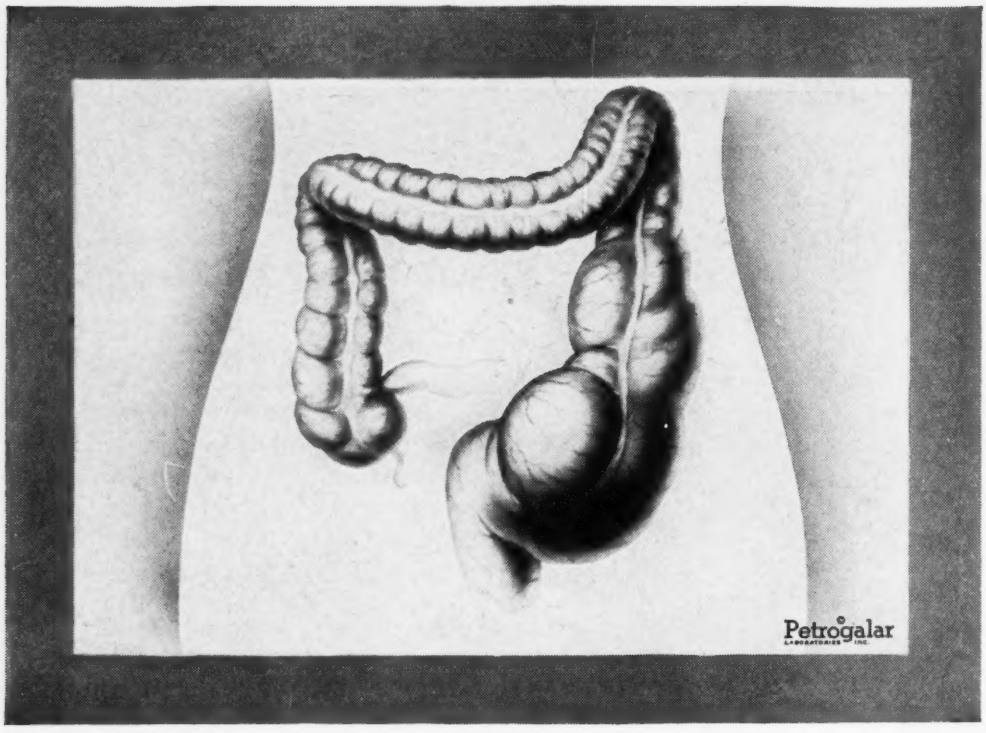

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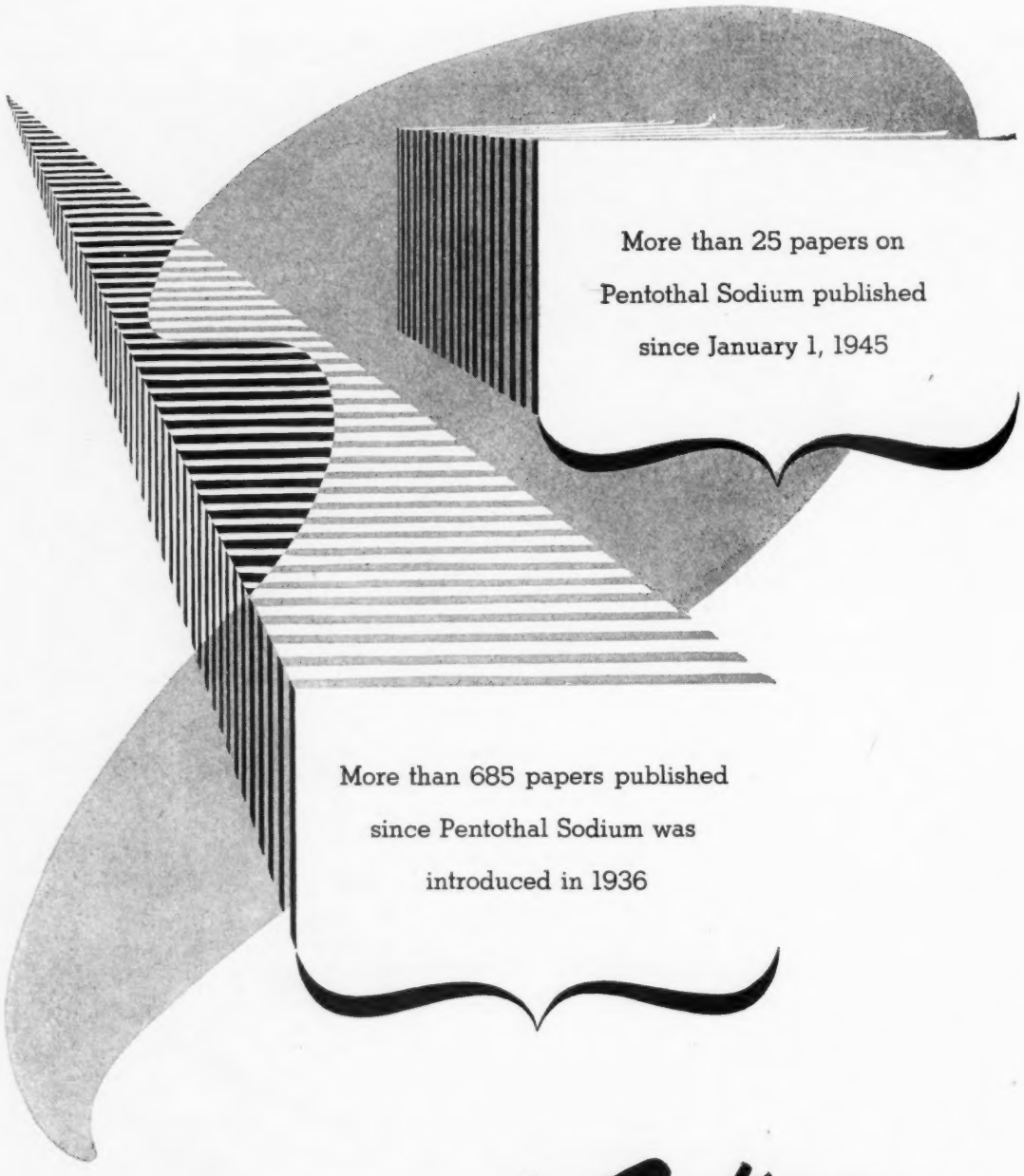
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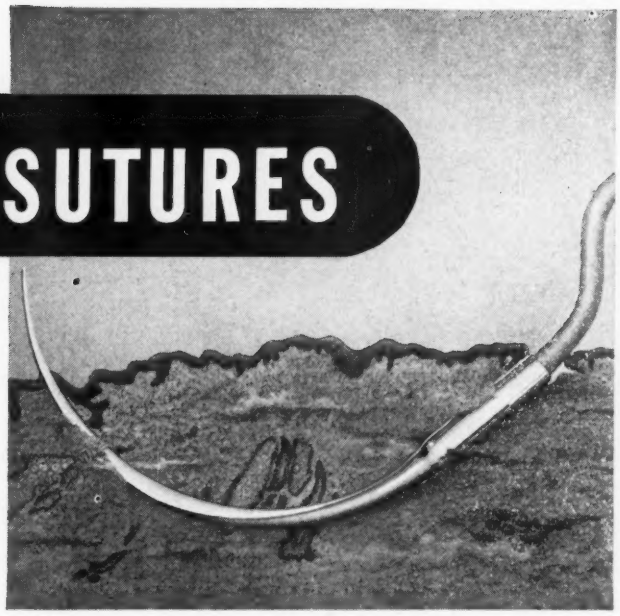

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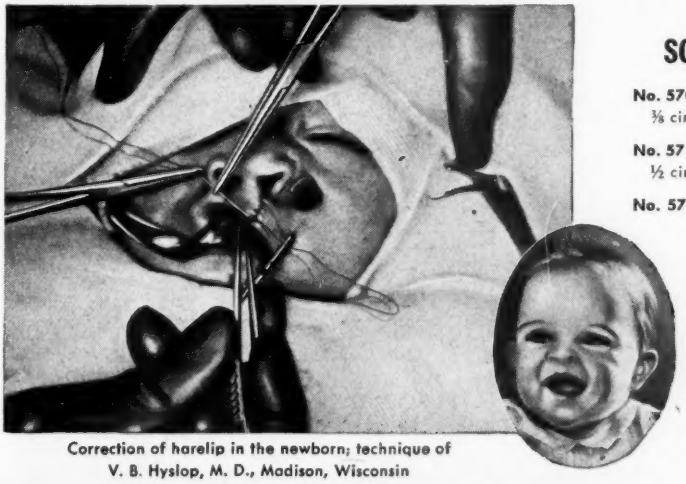

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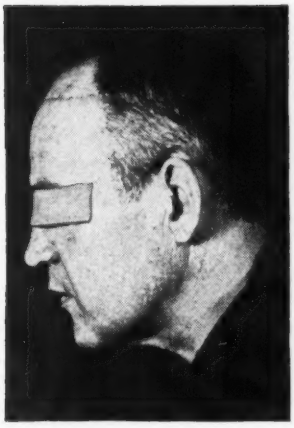

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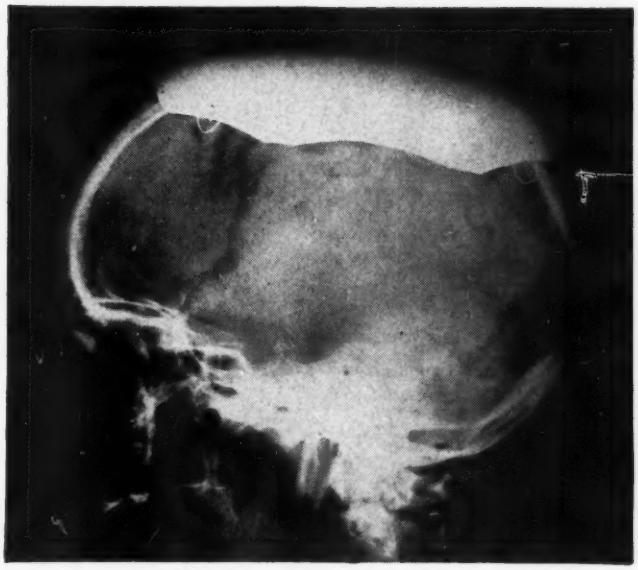

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SURGERY

VOL. 18 JULY, 1945 No. 1

Original Communications

Symposium on Anesthesia

FACTORS INFLUENCING TRENDS IN ANESTHESIA

JOHN S. LUNDY, M.D., R. CHARLES ADAMS, M.D., AND
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(From the Section on Anesthesiology, Mayo Clinic)

MANY factors have influenced the use of agents and methods in the production of anesthesia for surgical, obstetric, and dental patients. Obviously, one of the most important was the discovery of an agent or method. The work of Morton and Long gave ether anesthesia its start and the work of Horace Wells gave nitrous oxide its start. Other agents have been introduced in this first century of anesthesia and have influenced the trend in anesthesia practice, sometimes only briefly but sometimes very markedly. For example, Gwathmey's contribution of mixing oil and ether and later the introduction of tribromethanol in amylene hydrate (avertin) advanced the use of the rectal method very definitely. Several pioneers advanced the cause of local, regional, and spinal anesthesia. The contribution of the hollow hypodermic needle helped to make intravenous anesthesia possible. The vast amount of research on the various barbiturates resulted in the production of pentothal sodium, an agent that is extensively used today. The development of gas machines had a marked influence on the use of anesthetics, particularly the addition of the soda lime absorber for removal of carbon dioxide. Magill's contribution of his intratracheal tube was a landmark in the improvement of inhalation anesthesia. There are many other influencing factors that are perhaps less obvious, such as societies composed of those interested in the administration of anesthetics, periodicals and textbooks on the subject, and the organized teaching centers for clinical teaching and research.

The special circumstances and environment which characterize the various medical schools and hospitals throughout the country are very important factors with respect to anesthesia. The policy of the superintendent of a hospital may be reflected in the methods of anesthesia that are made available to the staff. For example, if the anesthetist can administer only inhalation anesthetics, then the surgeon must himself provide any other type of anesthesia that he would like to use. If the surgeon is only an occasional user of a method he may give it up as being unsatisfactory if he cannot carry it out well. Quite often the patient has a preference for a certain agent or may be antagonistic to a method. For example, many patients do not want to submit to ether

Received for publication, Aug. 12, 1944.

anesthesia and others refuse to submit to spinal anesthesia. Some patients are so excited that heavy doses of preliminary medication may be resorted to. This also influences one's choice of anesthetic and tends to make the use of ether by inhalation, for example, unsatisfactory.

The surgeon has, as a rule, a very definite opinion about the anesthetic of choice. Unless he reposes enough confidence and responsibility in the anesthetist so that the anesthetist may choose and use a certain anesthetic, the choice will be dictated by the surgeon. In time this factor will decrease the anesthetist's enthusiasm for maintaining his skill with a variety of agents and methods.

Anesthesia at the Mayo Clinic in the last fifty years has been influenced by a variety of circumstances that have been described elsewhere.[1] Ether and chloroform were first used. Nitrous oxide was used in 1900 but because of the fact that a heavy preliminary medication of scopolamine was used the color of the patient was unsatisfactory and the agent was not used again until 1918. At this time it was used for dental surgery and it has been used ever since for all types of operations.

When ethylene was introduced in 1923 it was used extensively at the clinic. Rectal anesthesia was given a trial in the early twenties. Magill's method of intratracheal anesthesia using the large bore, soft rubber tube was adopted in 1930. Cyclopropane was used in 1933. In 1929 the intravenous method of using sodium amytal was reported on and it was tried here in 1930. In 1931 one of us (J. S. L.) reported on the intravenous use of pentobarbital sodium (sodium nembutal). In 1933 evipal was used and in 1934 pentothal sodium was introduced here. Other agents that were not anesthetics, such as carbon dioxide, were employed from the beginning of 1924. Intocostrin for the production of relaxation, particularly for abdominal operations, was first used here in 1943.

Of the local anesthetics, procaine hydrochloride has remained the favorite, with metycaine hydrochloride a close second. Pontocaine hydrochloride and nupercaine hydrochloride have been tried and discarded. The introduction of Lemmon's method of continuous spinal anesthesia and Hingson's method of continuous caudal anesthesia has made it possible to obtain long-lasting anesthesia by repeated injections of procaine so that long-lasting anesthetics were not essential.[2]

As each agent and method has been introduced and tried, certain benefits were realized and certain unexpected and sometimes untoward results have been experienced. In consequence, there has been less tendency to advocate the use of any certain anesthetic agent or method and there has been a tendency to avoid strongly the use of certain drugs. For the most part, if a local anesthetic is used and is unsatisfactory it is then supplemented with gas anesthesia with or without intravenous anesthesia. If gas anesthesia is unsatisfactory, then usually one resorts to diethylether. In most cases the use of ether by the semi-open-drop method produces good results, especially if Magill's intratracheal tube can also be used.

The question is often asked of us: "Why do you use a certain agent or method so much or so little?" The simplest way to indicate the proper answer to such a question is to present the statistics that are available for the last twenty years concerning anesthetic agents and methods in our hands.

In Table I both the actual figures and the percentages are shown. The use of ordinary methods refers to ether by the semi-open-drop method; nitrous

TABLE I. COMPARISON OF USE OF SPECIAL AND OF ORDINARY AGENTS AND METHODS

YEAR	CASES			PER CENT	
	SPECIAL	ORDINARY	TOTAL	SPECIAL	ORDINARY
1924	1,169	16,370	17,539	6.7	93.3
1925	3,302	17,453	20,755	15.9	84.1
1926	3,478	17,782	21,260	16.4	83.6
1927	2,825	18,948	21,773	13.0	87.0
1928	3,163	18,412	21,575	14.7	85.3
1929	4,002	16,848	20,850	19.2	80.8
1930	5,662	13,930	19,592	28.9	71.1
1931	5,528	11,962	17,490	31.6	68.4
1932	4,218	9,685	13,903	30.3	69.7
1933	4,348	9,672	14,020	31.0	69.0
1934	5,779	10,639	16,418	35.2	64.8
1935	9,056	8,270	17,326	52.3	47.7
1936	13,397	5,503	18,900	70.9	29.1
1937	12,222	7,949	20,171	60.6	39.4
1938	13,411	7,843	21,254	63.1	36.9
1939	14,918	6,828	21,746	68.6	31.4
1940	15,428	6,739	22,167	69.6	30.4
1941	15,146	8,757	23,903	63.4	36.6
1942	17,997	6,551	24,548	73.3	26.7
1943	18,443	9,749	28,192	65.4	34.6

oxide with or without ether; nitrous oxide, oxygen, and ether; ethylene and oxygen with or without ether, and the use of procaine by infiltration or use of topical anesthetics by the surgeon or his assistant. Under the title of "special methods" are those in the application of which special personnel is employed: for example, spinal and regional anesthesia that is administered by the professional anesthetist, as well as intravenous anesthesia, intratracheal anesthesia, cyclopropane, curare, and so forth. In 1924 special measures were employed in less than 7 per cent of the administrations. In Table II it will be noted that in 1924 whatever special methods were used were those in which regional anesthesia was employed. In Table III it may be seen in the over-all survey of the use of the various agents in 1924 that they fall primarily into three groups: (1) local anesthesia, (2) ether by the open-drop method, and (3) gases with or without ether. This limitation in choice of anesthesia was one of the reasons for institution in that year of a change of plan on the part of the management of the Mayo Clinic looking forward to the time when there would be a large choice of anesthetics and adequate personnel for their administration.[3]

One of us (J. S. L.) undertook to start this program on March 27, 1924, and since that time several associates, assistants, and students have collaborated in the effort up to the present time. The surgical staff has been a major influence in this program and, as that staff has changed, certain changes in the program have occurred. The older surgeons had used ether by the drop method almost exclusively and some of the younger men without that experience were not so enthusiastic about ether as were their elders. Some wished to indicate the type of anesthetic to be used on every patient they operated on; others wished the Section on Anesthesiology to recommend what type of anesthetic should be used. In general, in spite of a gradual changing of personnel both in surgical staff and in the anesthesiology staff, certain agents and methods have been introduced from time to time and it has been the policy of the Section on Anesthesiology not to ride a hobby or encourage the use of any one agent or method to the exclusion of others. It was felt that if the agent or method had merit it would survive. The greater the merit, the more extensively would the method be used.

TABLE II. SPECIAL AGENTS AND METHODS, PER CENT

	1943	1942	1941	1940	1939	1938	1937	1936	1935	1934	1933	1932	1931	1930	1929	1928	1927	1926	1925	1924
Regional block*	38.5	37.2	37.9	40.4	39.5	39.7	42.1	38.5	58.3	79.9	81.1	80.8	86.7	83.8	79.1	95.2	94.4	99.1	99.8	100
Oil-ether colonic															0.2	3.9	5.1	0.8	0.1	
Acetylene														0.2	1.0	0.4				
Tribromethyl alcohol and barbiturates														0.03	0.09					
Barbiturates (by rectum)													0.01	0.4	0.4					
Barbiturates (intravenously)	35.8	38.9	42.6	43.5	39.8	31.2	31.5	20.4	14.9	2.6	0.3	0.6	1.4	8.9	15.2					
Tribromethyl alcohol	0.2	0.2	0.2	0.2	0.2	0.2	0.2		0.03	0.2	1.3	2.2	0.7	0.8	0.3					
Intratracheal anesthesia	18.2	18.4	15.4	13.8	13.9	13.1	12.1	8.0	10.2	14.8	16.2	15.5	10.4	5.2	2.9					
Intrapharyngeal anesthesia	2.4	2.4	2.2	1.1	0.23	0.8	0.2	0.2	0.1	0.3	0.2	0.6	0.5	0.7	0.3					
Cyclopropane	5.0	2.9	1.7	1.0	6.3	15.0	13.9†	32.6	16.3	1.7	0.3									
Divinyl ether							0.01		0.01		0.1									

*This decrease in the percentage of cases in which regional anesthesia was employed does not mean that there was a decrease in the actual number of cases in which it was employed, for in 1933 it was used in 3,537; in 1934, in 4,621; in 1935, in 5,271; in 1936, in 5,166; and in 1937, in 5,136.

†Fifty per cent of total number of administrations of cyclopropane are considered "special agent" and 50 per cent are considered "ordinary agent."

TABLE III. AGENTS, COMBINATIONS OF AGENTS, AND METHODS USED IN ANESTHESIA, PER CENT*

	1943	1942	1941	1940	1939	1938	1937	1936	1935	1934	1933	1932	1931	1930	1929	1928	1927	1926	1925	1924
Local (spinal excluded)	23.4	23.1	24.2	22.3	20.2	29.1	29.2	31.0	32.5	33.0	32.4	33.9	30.0	37.2	36.2	40.3	40.2	42.7	45.0	43.2
Local and ether (spinal included)	0.01	0.01	0.02	0.03	0.03	0.05	0.02	0.05	0.04	0.03	0.17	0.1	0.2	0.11	0.18	0.26	0.3	0.8	1.7	1.4
Local and gases (with or without ether; spinal included)	11.4	10.0	10.5	10.8	12.05	9.3	5.9	11.2	11.6	10.3	8.9	9.5	11.7	10.6	8.0	9.96	11.6	11.4	4.1	0.9
Spinal only	11.3	10.0	8.8	6.6	8.05	8.2	10.8	10.4	12.5	13.2	11.8	10.1	16.4	9.3	4.59	1.19	0.4			0.01
Ether (by open-drop method)	0.9	0.5	0.3	0.5	0.59	0.7	0.6	0.5	0.5	0.8	2.7	3.5	5.5	7.09	15.2	16.7	19.6	19.1	20.3	44.4
Gases (with or without ether)	29.7	30.8	27.6	27.6	28.9	31.6	30.8	31.7	34.8	41.4	43.4	41.5	35.1	30.6	31.0	30.1	26.9	25.3	28.4	27.6
Barbiturates, intravenously and rectally	13.6	14.4	15.5	17.2	19.9	19.7	17.9	13.4	6.6	0.8	0.07	0.1	0.1	0.11	1.24					
Tribromethyl alcohol	0.07	0.1	0.1	0.1	0.12	0.1	0.06		0.005	0.03	0.07	0.05	0.01	0.09	0.009					
Ethyl chloride (as general anesthetic)										0.01		0.007	0.02	0.01	0.27	0.26	0.08	0.1		0.5
Oil-ether colonic															0.57	0.58	0.6	0.1	0.01	
Chloroform																	0.3	0.1	0.09	

*This table includes only those cases in which the agent, combination, or method named was the only one used; that is, unless otherwise indicated.

The results are apparent in these three tables. In Table I it will be noted that special agents and methods have come to be used in about two-thirds of the cases. Ordinary agents and methods are used in about one-third of the cases and this has been true for the last seven or eight years. In Tables II and III it will be seen clearly that a mixture of oil and ether by rectum has been used but little. It has not been used at all for the last fourteen years. There were several reasons for discontinuing the use of oil and ether by rectum. The anesthesia was not always satisfactory, the method did not fit into the general scheme of things utilized by local hospitals for the handling of patients, that is, bringing them to the operating room in a wheel chair and so forth, patients often expelled some of the agent, the dose had to be guessed at and might be either too much or too little, and the percentages of such cases were high enough so that the method was not uniformly satisfactory. These remarks should not be construed to mean that it is not possible to anesthetize a fairly high percentage of patients by this method with considerable satisfaction if an experienced anesthetist is available and can devote his full attention to one case at a time. However, while it is not a mortal reflection on the method that it requires the full attention of an experienced anesthetist throughout the period of administration, nevertheless such a method is not economically as desirable as some other method in which one experienced person can supervise its use in the hands of several less skilled persons. It is used only rarely for surgical cases now but is occasionally useful in anesthetizing patients suffering from an attack of intractable asthma.

Tribromethyl alcohol as a rectal anesthetic was used here in 1929 and was more satisfactory than oil and ether by rectum. The use of barbiturates by rectum plus tribromethyl alcohol was tried but did not have any apparent advantage over tribromethyl alcohol itself and this combination was used but for a short time.

A different situation concerned the use of acetylene. It was used a few times in 1928, 1929, and 1930. About the same time it was being used in Germany under the name of narcylen. The advantages of the method were that the use of ether could be avoided and large quantities of oxygen could be administered. The hazard of explosion was very great and for that reason its use was discontinued. Since that time other agents and methods have appeared which make it neither necessary nor desirable to use acetylene again.

The intravenous use of barbiturates was begun in 1929 with sodium amytal. The results were both encouraging and discouraging. The patients liked the method but the postoperative restlessness was too great. In 1930, pentobarbital sodium (sodium nembutal), another barbiturate, was tried. Although for a time it seemed to be better than sodium amytal, still the results were not satisfactory so that by 1933 the intravenous method was practically not being used. In 1934 we began the use of pentothal sodium and since 1937 it has been employed in about one-third of all cases in which special methods of anesthesia were used. It seems that, now that the method is rather thoroughly established, its usefulness is fairly well known and its percentage of use does not vary much from year to year.[4] This, as in the case of other agents and methods, would indicate a joint opinion of surgeons and anesthetists on this point in this institution.

Divinyl ether was tried in 1933, again in 1935, and again in 1937 in a few cases, but it had no advantages from our point of view over intravenous anesthesia and so it has not been used for the last six years. Cyclopropane,

use of which was begun in 1933, has had a considerable change in percentage of use from time to time. The explosion hazard is well recognized and there are some other effects cyclopropane seems to have on some patients that have made us guarded in the use of it, namely, sudden collapse at the end of the operation when the anesthetic was discontinued in some very prolonged and major procedures. We have heard about such episodes from others but have seldom observed them ourselves. The reports of fibrillation due to the drug have made us cautious, although actually we seldom have encountered this result clinically. It would appear that, if one observes the recommended precautions[5] in the use of cyclopropane, it is a widely useful agent but it is not an essential except in a limited field, particularly thoracic surgery.

One oustanding method begun in 1920 was the use of Magill's intratracheal tube. Its use has greatly enhanced the value of the inhalation anesthetic agents and has provided an adequate airway under almost all circumstances in which improvement in patency of the airway was needed. The intratracheal method has survived vicissitudes associated with the placing of the tube, which involved in some cases broken teeth or trauma to the respiratory passages or both.

Such agents as chloroform and ethyl chloride by inhalation have not survived because of the fact that the risk of death associated with their use was considered to be unjustified because there are now other kinds of agents for anesthetizing patients in cases in which these agents previously were used.

From Table III it is seen that for the last eight years there has been little change in the percentage of employment of the agents used at present. It has been the joint experience of the anesthetist and the surgeon that under the circumstances under which we work, which are all-inclusive, we get our best all-around results by using certain agents and methods with the indicated frequency. We do not consider that our use of these agents and methods is necessarily the best use of them elsewhere. We recognize that in the various other medical centers there are definite reasons for using various agents and methods differently than is done here.

Many factors are involved in the choice of anesthetic which cannot be elaborated here, such as the speed that various operating surgeons employ in one institution as compared with another, the necessity for well-organized and co-ordinated work on the part of both the anesthetists and the surgeons for the satisfactory handling of a large number of patients, an abundant supply of materials and personnel in contrast to a lack of these things, and the personal enthusiasm or prejudice of either the surgical or anesthesiologic staff for or against a given agent or method. All these things make for a difference in statistics in different institutions. It does not seem necessary to argue that one institution is wrong if it does not follow the lead of another.

One agent about which there might be controversy may be selected as an example for discussion. The one selected will be diethyl ether by inhalation with or without the use of an intratracheal tube. In Table III it will be seen that there has been little change in the frequency with which ether was used for the last eight or nine years. However, if a visitor happens to observe during a period of a few days when ether is used frequently by the open-drop method, he may gain the impression that this is the standard practice although actually the agent may have been used oftener at that particular period than at any other time during the year. If ether were obviously undesirable in the cases in which it has been used, even though this conclusion might not have

been very clear twenty-five years ago, it would have become very clear now or in the last few years. Since practically any agent or method that is available anywhere is available here and since the members of the staff visit other institutions and attend meetings, they have the opportunity to see the results obtained elsewhere and after discussing the results observed elsewhere they may decide to try that technique here. This has been done repeatedly with practically all combinations of anesthetics and if the results then obtained were superior to those obtained previously then the method has survived and the old one is abandoned. In examining the figures in Tables II and III it must be clear at least for the last several years that the agents and methods employed and the methods of administration have been generally satisfactory to those concerned. The figures show more trend to use special methods whenever these methods have given better results than were obtained with ordinary methods.

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EXPLOSIONS IN ANESTHESIA

A Review of the Literature

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EXPLOSIONS have been witnessed by many anesthetists and surgeons and the danger of their occurrence is surely well known to those physicians in whose presence they have not yet occurred. It is unfortunate, as LeeRoy and Sword[1] have written, that almost all inhalant anesthetic drugs used today will burn or explode; further, that they are always given with air or pure oxygen; and that these mixtures are confined in closed spaces in the anesthetic apparatus and in the patient's respiratory system. The various ethers, ethylene, and cyclopropane have been involved in numerous fires and explosions. Nitrous oxide has been exonerated only in the laboratory. It is stated to have been the sole anesthetizing agent in the instance of an explosion described in 1924.[2] The gas was reported to be a mixture of nitrous oxide and oxygen; the source of heat, the high frequency electrical cautery. On touching the patient with the electrode, an explosion took place in the gas mask and rubber tubes. It was theorized that "the explosion occurred by reason of the fact that some carbon or foreign substance had got into the nitrous oxide and oxygen gas being used." According to Luckhardt,[3] a nitrous oxide-oxygen mixture can be ignited and thus exploded by a thermocautery. Herb,[4] substituting nitrous oxide-oxygen for ethylene-oxygen, reported two explosions "with this gas" within a few

Received for publication, March 12, 1945.
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weeks. Ether was present in the ether chamber of the gas machine when these explosions occurred; it became ignited "in one of the nitrous oxide-oxygen explosions." Wilson, in discussing an article by Blomfield,[5] described two cases of fatal explosion in England associated with nitrous oxide anesthesia; a bronchoscope was used in one case, a flame reached the patient's mouth in the other. The explosion of a tank containing nitrous oxide was reported in 1929[6]; the tank was on the floor, disconnected from the machine, and its valve was being manipulated at the time of its explosion. It was assumed that the tank contained some ethylene, as the machine in the operating room on the occasion of the explosion was not equipped with a device rendering impossible the mixture of these gases; there was no further evidence for this assumption. The *British Medical Journal*[7] referred, in 1935, to "explosion limits" of nitrous oxide, to the "ready ignition" of this gas, and warned that it was not to be regarded as inert. Livingstone, Shank, and Engel[8] reported, in 1939, three so-called nitrous oxide-oxygen explosions, one in Missouri (urethral caruncle cauterization) and two in England (both during the use of a bronchoscope); they suspected the presence, in the apparatus, of ether or oil or, in the nitrous oxide, of carbon or "foreign substance." Greene[9] reported, in 1941, an explosion of nitrous oxide-oxygen "plus unknown." Pinson[10] reported "alleged explosions of chloroform vapour." Kretschmer[11] reported two explosions, in 1934, occurring during transurethral electroresection of the prostate under sacral anesthesia. He added, "Practically every urologist, during the course of fulguration treatment of bladder papillomas has at some time or another experienced small intravesical explosions." The explosive mixture in these cases, where no combustible gas has been administered, is hydrogen-oxygen, products of hydrolysis of water in the bladder by the action of the electric current.

HOW GREAT IS THE DANGER?

"The total number of ethylene fatalities," wrote Williams[12] in 1930, "has not been large. Were there no remedy it might even seem proper to continue its use in the manner and with the equipment hitherto employed." Henderson,[13] writing in 1930, defended the anesthetic apparatus of the day, stating that explosions caused one death in about 100,000 anesthesias, and that, in comparison, other commoner hazards consequent on older methods of anesthesia were greatly reduced. He said that ether is responsible for more explosions or flares than ethylene and concluded: "Explosion is today the least of the hazards of anesthesia." "Respiratory complications and shock from improperly administered anesthetics," wrote Griffith in 1931,[14] "cause a hundred times more deaths than all the explosions." One fatal anesthetic explosion receives widespread attention, the *Journal of the American Medical Association*[15] declared editorially, while 100 deaths from postoperative pneumonia may go unpublicized. Herb[16] listed the reported explosions in 1933 as follows: ethylene, 20 explosions with 5 deaths; nitrous oxide-oxygen-ethylene, 2 deaths; nitrous oxide-oxygen-ether, 39 explosions with 5 deaths. She asserted that 20,000 anesthesias were given with no explosion, following the installation of a conductive grounded floor; she had reported,[4] in 1925, 5 ethylene explosions in about one and one-half years at one hospital, occurring in what was later referred to as a few hundred anesthesias. Phillips,[17] writing in 1936, believed that the danger of anesthetic explosions was great. With the advent of ethylene, wrote Guedel[18] in 1937, "we became explosion conscious." An editorial[6] of the *Journal of the American Medical Association* (1939) estimated the frequency of ether accidents

at about 100 a year. "Ether anesthesia," it said, "is too well established to be affected by explosions, which are usually not even reported." The Subcommittee of the American Society of Anesthetists on Fires and Explosions[19] listed all reported explosions for the fifteen-year period from 1925 to 1939 as follows: ether-air, 23 explosions with 2 deaths; ether-oxygen, 10 explosions with 3 deaths; nitrous oxide-oxygen-ether, 19 explosions with 9 deaths; ethylene-oxygen, 16 explosions with 5 deaths; cyclopropane-oxygen, 9 explosions with 3 deaths; cases in the last two groups included those in which ether or other agents had been added. Woodbridge,[20] writing in 1939, suggested that the explosive risk was very small, in proportion to the other risks attending surgery and anesthesia, and that the dramatic nature of an explosion was largely responsible for the publicity and fear associated with this hazard. He asserted that the explosion rate was about 2 to 4 per 100,000 administrations; this was based on 64 explosions occurring in 2⅓ million anesthesias, with 2 deaths. Pinson[10] asserted that at least 100 ether explosions probably occur in England annually. Livingstone, Shank, and Engel[8] offered, in 1939, the findings of 6 collections of anesthetic explosions. The first study was by Herb, who, they stated, reported (in 1930) 1,005,375 ethylene anesthesias, with 20 explosions and 5 deaths. The second study reported by them was that of Henderson, in which ethylene anesthesias at 288 hospitals resulted in 10 explosions and 1 death. Their third group of cases was reported by Cabot; 146,000 ethylene anesthesias given at 75 hospitals resulted in 1 explosion and 1 fire. Their fourth list was based on the reports of 58 surgeons, according to which more than 163,000 ethylene anesthesias resulted in 18 explosions and 1 death. The fifth group cited by these authors was that of Salzer who, in 1929, reported 425,000 ethylene anesthesias with 10 explosions and 1 death. The sixth collection offered by Livingstone and her colleagues was as follows: ether or ether-oxygen, 34 accidents; nitrous oxide-oxygen-ether, 14 explosions; ethylene-oxygen, 14 explosions; cyclopropane-oxygen, 11 explosions; oxygen, 9 accidents; nitrous oxide-oygen, 3 explosions; there were 27 deaths in this last series. Horton[21] stated, in 1941, that anesthetic explosions were rare. Greene[9] reported, in 1941, a collection of 230 anesthetic fires and explosions.

Injuries to the patient usually include burns, rupture of the lungs, and trauma from flying metal and glass. Greene[9] was able to report 3 cases of recovery from ruptured lungs.

ARE THE RISKS DIFFERENT FOR DIFFERENT COMBUSTIBLE AGENTS?

Luckhardt and Lewis,[22] writing in 1923, in one of the earliest articles describing the anesthetic properties of ethylene and its use in man, warned of its inflammability and explosibility. Henderson[13] stated, in 1930, that ether is responsible for more minor explosions or flares than ethylene, but that ethylene explosions are more violent. Luckhardt[3] believed ethylene-oxygen mixtures to be no more dangerous from an explosive standpoint than ether-oxygen mixtures. The Council on Pharmacy and Chemistry of the American Medical Association reported,[23] in 1939, that it considered cyclopropane to have the same potential explosion hazard as ether and ethylene. Woodbridge[24] concluded from his study of 2⅓ million anesthesias that ethylene, cyclopropane, and ether (given with oxygen or nitrous oxide) are equally dangerous from the explosive standpoint, and that drop ether is safer. Horton[21] declared, in 1941, that the rarity of anesthetic explosions rendered statistics "inadequate to show whether one gas is relatively more dangerous than another, or whether there is an increasing fre-

quency of occurrence of anesthetic explosions." Greene[25] attributed the apparent safety of ether to "the relative harmlessness which is associated with the combustion of any anesthetic mixed with air."

SHOULD ANY GAS BE BANNED?

Griffith[14] warned, in 1931, that going back to ether-oxygen or to nitrous oxide-ether-oxygen had without justification given several workers a feeling of security and had made them neglectful of the usual precautions to be taken when working with explosive mixtures. Woodbridge quoted Guedel, in 1939,[20] to the effect that prohibiting the use of ethylene or cyclopropane was ridiculous. Poe's opinion[26] on the banning of ethylene (1930), typical of most physician-anesthetists, is worth quoting: "To discard ethylene in anesthetic is like discarding the use of gasoline in transportation, because some persist in using a match to see if the tank is empty."

IS ETHER DANGEROUS?

That ether mixtures will explode has been pointed out by many investigators. That the likelihood and violence of such explosions are increased by the substitution of oxygen for air in ether mixtures has been stressed in many articles. Black[27] reported, in 1874, a relatively harmless ether fire initiated by the actual cautery used in removing a tumor of the neck; other ether fires and explosions very likely happened before this. An ether explosion was reported as early as 1892,[28] in England; ether upset near a fireplace became ignited and exploded, shaking the house, breaking windows, and demolishing the room. Brown[29] stated, in 1924, that nitrous oxide-oxygen-ether mixtures were as explosive as ethylene-oxygen mixtures. Writing in 1928, Lundy[30] declared that the flash points of ethylene and ether are about the same. Poe[26] warned, in 1930, of the danger of administering ether-oxygen by insufflation because of the great violence of ether-oxygen explosions, and, it is assumed, the likelihood of the occurrence of an explosion with this technique; at the same time, however, he recommended the practice of performing ethylene-oxygen anesthesia with nitrous oxide induction, a procedure regarded as dangerous by later writers. Guedel[18] stated that the substitution of oxygen for air in ether anesthesia increased the speed of flame propagation into the lungs and heightened the violence of the explosion. Livingstone, Shank, and Engel[8] have said that ether explosions have occurred during anesthesias in which this agent was given by the open-drop method, by motor-driven ether vaporizers, and by various machines in combination with oxygen; that the source of ignition has on different occasions been turning on an electric light, the laryngoscope, cautery (in one instance, during a hemorrhoidectomy), static spark, electric penlight, cigarette, diathermy electrode, motor blower, fulguration tip, operator's headlight, fluoroscope, suction motor, and the bronchoscope. In their discussion of nitrous oxide-oxygen-ether mixtures, these authors have well said: "The very presence of this mixture in an apparatus, whether or not it is in use, is to be treated with great respect." Woodbridge, Horton, and Connell[31] warned, in 1939, that ethyl and vinyl ethers and ethyl chloride are explosive in air, oxygen, and nitrous oxide. Newcomer[32] emphasized, in 1940, the explosiveness of ether-oxygen mixtures, adding that they ignite at even lower temperatures than cyclopropane-oxygen. "The ether explosion hazard," wrote Morrill[33] in 1941, "very closely approximates that for ethylene." Ether-air mixtures, Greene[9] stated, have produced fatal explosions but they tend very little to propagate "a wave of flame or pressure into and down the respiratory tract"; ether-oxygen, however, with

or without nitrous oxide, has as great a tendency to do this as has ethylene-oxygen or cyclopropane-oxygen. Morgan[34] stated, in 1931, that while ignition temperatures of hydrogen, carbon monoxide, and methane are about 500° C., ether vapor will ignite at about 190° C., and that "liquid ether when contaminated by impurities may ignite at a temperature as low as that of boiling water." "From time to time," wrote Featherstone[35] in 1931, "I hear of a minor 'pop' having occurred when a small lighted electric bulb has been inserted into the mouth during ether-air anesthesia." Commenting editorially on an ether explosion in 1903, the *Lancet*[36] stated that "it is well known that a mixture of ether vapour and atmospheric air is highly explosive."

HOW DOES AN EXPLOSION OCCUR?

The conditions necessary for an explosion are, as Rovenstine[37] has well stated them, "an inflammable gas vapor or other substance; oxygen, either pure or in the air, or a gas or other substance that provides oxygen, such as nitrous oxide; and a source of ignition." It is, therefore, easily understood that attempts to solve the problem of anesthetic explosions would be directed toward the elimination of each of these three conditions. Two other types of explosion, due to (a) pressure and (b) the presence of a spontaneously combustible mixture, will be referred to later.

IGNITION

The sources of heat serving to ignite combustible mixtures are numerous, as many investigators have listed them. The dangers of the open flame and cigarette have long been recognized. The hazard of the actual cautery has long been known and, more recently, the dangers of the electric cautery, diathermy, and x-ray apparatus have come into widespread knowledge. Greene[9] reported, in 1941, a collection of 230 anesthetic fires and explosions. Of these, x-ray apparatus was involved in 10 cases, cautery apparatus in 57 cases, diathermy apparatus in 20 cases, suction-pressure machines in 59 cases, endoscopic apparatus in 5 cases, and static electricity in 63 cases. The ignition point of a combustible gas, according to Pinson,[10] is the temperature at which it "fires." "The term 'flash point,' refers to a liquid," he wrote, "being that temperature at which it gives off inflammable vapour." Adriani[38] defined flash point as the "lowest temperature at which vapor of a liquid may be ignited"; kindling temperature as the "lowest temperature at which a combustible mixture ignites and continues to burn per se." According to Cooper,[39] the flash point, which indicates the ability of a liquid to form explosive mixtures, is the temperature to which the liquid must be heated to produce a flash or flame when a small flame is passed across the liquid's surface. Ethyl and vinyl ethers, he pointed out, have very low flash points and can thus form explosive mixtures in oxygen or in air at temperatures below 0° F. A sufficiently large portion of a gaseous mixture, he wrote, must be heated to its ignition temperature, that temperature at which rapid combustion becomes independent of external supplies of heat, and that temperature must be maintained until ignition occurs in order that the mixture be exploded. Any combustible, he added, when mixed with oxygen will ignite at a lower temperature than when mixed with air; the difference is not usually great but it amounts to more than 100° C. for ether. According to Blomfield,[5] the rapid ignition point of ethylene in oxygen is 604° C., "a temperature at which a solid body is just visibly red in a dark room"; proportions of the gases were not given. He further stated that (a) raising the pressure caused a lowering of the ignition point; (b) reducing "the presence

of the oxygen'' produced an initial rise in the ignition point, then a lowering of this temperature, and finally a noncombustible mixture; (c) the ignition point of ethylene is lower in nitrous oxide than in oxygen. Dixon[40] warned, in 1926, of the danger in bringing a heated body in contact with an ether-oxygen mixture. ''That the heated body is not visible red-hot,'' he wrote, ''is no guarantee of safety; the danger point begins at least 300° C. below visible redness.'' Pinson[10] stated, in 1930, that visible red heat is necessary to ignite an ether-air mixture. Ether-oxygen mixtures can be ignited, according to Cooper,[39] at 184° C., a temperature well below a visible red heat.

Greene[9] stated, in 1941, that ''most anesthesias by insufflation today are still being administered in the presence of serious, obvious and preventable sources of ignition''; he called attention to the large number of accidents (more fires than explosions) and to the small number of injuries and recommended (a) mercury switches, (b) sealed motors, (c) grounding the metal cabinet, and (d) high, locking wall outlets.

ELECTRICAL EQUIPMENT

The existence, location, and condition of such obvious sources of ignition as outlets, switches, wires, terminals, cautery, high frequency apparatus, and lamps are usually obvious and should be known by the entire operating room personnel. Phillips[17] listed, in 1936, the following as the usual electric circuits and equipments that are dangerous in the operating room: lights and light fixtures, receptacles and attachment plugs, all switches, all rheostats and adjustable transformers, cords to portable and semiportable equipments (in fact, all exposed cords and wires), electric sterilizers, cauteries, electrically illuminated lights, diathermy, fulguration, high frequency, x-ray, and fluoroscopic equipment, electric motors (suction devices, bone saws), electrocardiograph, telephones, buzzers, telephone magneto-ringers. He pointed out three dangerous features of the electric cautery: (a) the heat deliberately generated, (b) the frequent sparking of the rheostat or transformer used to regulate the temperature, and (c) the possibility of breaking or separation of cords and terminals with arc formation. All electrical circuits in the operating room, Tovell and Friend[41] wrote, in 1942, should be supplied by insulated transformers outside the room; the three-wire type of wiring should be used, they stated, the third wire serving to ground all housings. They emphasized the importance of safety type switches, receptacles, plugs, motors, and lighting fixtures.

Greene[9] collected five combustions due to electrically lighted instruments, as the bronchoscope, laryngoscope, and pocket flashlight; these were attributed to faulty contacts, poor insulation, breaking of bulbs, and short circuits. He recommended solid glass bulbs, low voltages, and properly functioning apparatus.

THE STATIC SPARK

Static spark is a more elusive source of ignition. Its location is not fixed, its occurrence cannot be predicted, and the conditions necessary for its creation are not perfectly understood by all workers.

The manner of formation of electrostatic charges has been described by many authors. Separation of insulating materials such as fabrics and rubber sheets, percussion, and friction (as in the breathing bag) are known to be common generators of static charges.

Horton[55] stated, in 1939, that a person wearing cotton garments could acquire a potential of more than 400 volts by moving about on a cushioned steel;

wearing street clothes increased the potential to several times this figure. He found fabrics to be responsible for most of the other sources of potential in the operating room. Merely draping the patient gave him a potential of about 40 volts to ground; inserting pads between the sterile sheet and the neck raised the patient's potential 150 volts; removing the instrument tray stand from the foot of the table gave the patient a potential of 50 volts. Farrand[42] asserted, in 1939, that a nurse "may in the course of an errand pick up a charge of several thousand volts"; he showed that manipulation of and breathing into the breathing bag generated from 200 to 1,000 volts, that turning a rubber-covered pad on an operating table generated about 6,200 volts.

In considering electrostatic charges, Newcomer[43] pointed out the fact that the capacity of the storing body, as well as its potential, is important, and that the potential does not alone indicate, under given conditions, whether or not a spark will incite an explosion.

According to Finch,[44] currents carried by the discharge produced at the breaking of an electric current are usually less than 1 amp. The rate of energy dissipation is low, he added, but the total amount of energy may be large if the discharge is prolonged over a considerable fraction of a second. The rate of energy dissipation in the case of static spark, he stated, is enormous, but is maintained for only a fraction of a millionth of a second. Several investigators, according to E. T. Jones,[45] have been of the opinion that spark ignition of an inflammable gas mixture was due, not to the heat developed, but to the current itself, or its ionizing effect, in the gas. Jones showed, however, that the ordinary spark is a better igniter than the condenser spark (in which the current crossing the spark gap is greater) and inclined to the thermal theory of spark ignition, that ignition depends on "the volume of the gas which the spark can by its own heat raise to the ignition temperature."

The electrical effect of the passage of gas through breathing tubes has been commented upon by many writers. Phillips[17] asserted that the flow of dry gases through rubber tubing will produce static charges. Luckhardt,[3] writing in 1924 of the possibilities of explosion, from ignition by a static spark, of ethylene-oxygen mixtures in the tubing, considered the mechanism of such spark formation to be largely or entirely the "development of static electricity as the result of the long-continued flow of an ethylene-oxygen mixture in the tubing." Williams[12] asserted that passage of dry gases through rubber tubing which is dusty or contains metallic powder from valve wear may create charges of several thousand volts in a few seconds. He further contended, in 1930, that the inside of the breathing tubes and bag is not kept moistened by the water vapor in the patient's exhaled breath; the compressed gases, he maintained, are made dry and adsorb water "with great avidity." According to Brown,[29] static sparks formed by a charge generated by the passing of a gas under pressure through a narrow orifice (the only method of spark formation in the operating room considered in his article) are not likely to produce an explosion. Sise[46] believed that ethylene flowing over rubber could generate a static charge. Wardell[47] asserted that the passage of gas may create static charges, if some particles of dust or liquid are present. The matter of liquid particles has been mentioned by several writers, and it is food for thought that their presence has been considered a factor in the production of static and at the same time a method of dispersing such charges. Rayner[48] advised, in 1938, blowing off a little oxygen before starting a new tank, to remove water or dust particles, which might cause the formation of static during the high rate of flow of the gas. McDiarmid[49]

quoted Kelvin to the effect that bubbling air through water causes the air to acquire a negative electrostatic charge. Knowing that the interfriction of solids produces a measurable electrical charge, she investigated the possibility of the production of electricity by the friction of gases on solids. Air was passed through tubes constructed of different materials (insulators: glass, quartz, ebonite; metals: iron, copper, brass, aluminum; rubber was not tested) and of different bores and lengths. She found that (a) charges were developed on the air and on the tubes; (b) the charge on the air was opposite in sign to that on the tubes; (c) the signs of the charges on the tubes were positive for some insulators and for some metals and negative for other insulators and other metals; (d) the charge developed on the air was directly proportional to the length of the tube; (e) electrification increased with the speed of flow; (f) wider tubes produced greater charges, as they permitted a greater speed of flow; (g) the greatest deflection of the electrometer needle, calibrated at 300 to 600 mm. per volt, was 950 mm., which would thus correspond to a charge of about 1½ to 3 volts; this was produced by a 5¼ second flow through a 10 mm. bore glass tube 78 cm. long, which would thus correspond to a rate of flow of about 695 c.c. per minute; the potential to which a metal container was raised, into which the air was conducted, was of the order of magnitude of 1 volt. No gas other than air was tested. It would thus seem that the charges created in this manner are too small to be significant in the etiology of explosions of anesthetic gases by static spark.

IS THE MACHINE THE OFFENDER IN STATIC FORMATION?

That a good part of the danger of electrostatic charge formation arises from the anesthesia apparatus itself has been contended by several authors. The theory of static charge formation by the movement of gas through the anesthesia apparatus has already been discussed.[3, 12, 17, 29, 46-49] Phillips[17] stated definitely that the anesthetic machine, with its breathing bag, tubes, and mask, constituted "the greatest single explosion hazard." Apart from the newest machines, equipped with conductive rubber throughout, Greene[9] was unable to find, in 1941, any apparatus "which can claim a real superiority with respect to the hazard of static production within the apparatus." He concluded, from a study of 63 static explosions, that the greatest danger lay in the anesthesia apparatus itself, with its breathing bag, tubes, and mask. Other investigators have felt, however, that little or no danger of static spark formation is created by the anesthesia apparatus itself. Connell,[50] representing the manufacturer of anesthesia apparatus, maintained, in 1939, that most static in the operating room is created by the unit including the patient, drapes, and attendants; less static, he felt, is generated by the anesthetist, and least by the apparatus. Used properly, the anesthesia machine, according to Horton,[21] does not contribute to the cause of ignition; he warned, however, of the danger inherent in the practice of removing the breathing bag during anesthesia and in the use of metal collars on breathing bags. Rayner[48] was of the opinion (1938) that charges responsible for explosions were developed outside the anesthetic apparatus. Lee-Roy and Sword[1] declared, in 1942, that "the possibilities of fire or explosion originating within the anesthesia apparatus and the patient's respiratory tract are remote for two reasons. Firstly, we do not always have a mixture that is easily ignited. Secondly, there is little if any possibility of ignition from within."

Griffith[14] regarded static electricity as the commonest source of ignition in anesthetic explosions. Static electricity was the commonest ignition source in

Greene's series[9] of 230 fires and explosions, where it was reported to have been the igniting agent in 63 of the accidents. An analysis of these explosions showed that static explosions occurring during anesthesia with ether-oxygen, ethylene-oxygen, or cyclopropane-oxygen almost invariably result in an injury to the patient, and that static ether-oxygen explosions often kill him.

EFFORTS TO REDUCE THE DANGER OF STATIC SPARK

As has been shown by many investigators, the presence of water vapor in the atmosphere serves to dissipate electrostatic charges on all bodies within its reach; the air or gas mixture is rendered somewhat conductive and charges tend to leak away from bodies on which they are generated, so that spark formation becomes less frequent or may not occur at all. Griffith[14] believed, as he wrote in 1931, that a static spark could not be produced in an atmosphere with a relative humidity of 54 per cent or more. He considered humidification to be the most effective method of eliminating static, and with it most of the anesthetic danger. Henderson[13] recommended, in 1930, a high relative humidity in the atmosphere of the operating room and moistening the gases inside the machine. Woodbridge, Horton, and Connell[31] employed other precautionary measures, but stressed the importance of humidification in the operating room. Wiggin[51] recommended humidification above 65 per cent. Sise,[52] in 1933, regarded humidification as the best safeguard against static spark.

Rovenstine,[37] writing in 1939, favored the practice of humidification. According to Cooper,[39] a relative humidity of 60 per cent or more in the operating room will eliminate the formation of static charges except within the gas machine itself; rinsing tubes, mask, and bag before anesthesia will increase the humidity inside the apparatus, he wrote. Draper,[53] too, conformed to the theory that moisture in the atmosphere dissipates static charges. Of 63 static explosions, Greene[9] found the relative humidity to be 60 per cent or more in 2 cases, 54 to 55 per cent in 3 cases, less than 50 per cent in 32 cases, not reported in 26 cases; of the 46 cases in which the seasonal incidence was given, only 2 occurred in the summer (when the humidity is high). He could find no reported static explosion in Australia and only one in England (the humidity in this case had been artificially established at a low level). He felt that humidification would not prevent all static formation, but that it should, nevertheless, be used. Phillips[17] asserted that humidification dissipates charges more efficiently than wiring, since the water reaches all surfaces.

The effect of humidity on the incidence of static explosions is borne out by Petavel's assertion[54] that the risk of static explosions is not great in England, where the atmosphere is not very dry; static explosions are rare in Australia and in England, where only one such accident has been reported. As Rayner[48] has well put it, "very cold, dry weather produces the worst conditions, for the outside air contains little moisture, and when it is heated the relative humidity becomes low."

The practice of humidification has not been without its opponents, however. Newcomer,[32] writing in 1940, did not believe that humidification would guard against static spark. The disadvantages associated with the maintenance of a high humidity, as Herb[16] has stated, are twofold: the constant attention necessary for the carrying out of such a program with the dangerous possibility of an unobserved fall in the relative humidity, and the discomfort experienced by an operating room personnel working in a high humidity in a warm room. Finch,[44] in 1935, considered humidification "not likely to be of much use." Fol-

lowing the occurrence of at least one explosion believed due to electrostatic discharge in an atmosphere whose relative humidity was 65 per cent, Horton[55] showed, in 1939, by means of electrostatic potential measurements and by the production of actual sparks, that a relative humidity of 65 per cent does not fully protect against electrostatic sparks. Connell[50] expressed the opinion, in 1939, that the danger of static spark cannot be entirely eliminated by increasing room humidity; he called attention to the formation of lightning "in the wet air of thunderheads by the violence of gusts and water droplets." He agreed, however, that high humidity is of value and declared that the water content is raised after three breaths in a closed circuit, and that the circuit is drenched within one minute. The importance of the carbon dioxide content of the atmosphere in rendering the air more conductive by raising its electrolyte concentration was stressed by Tovell and Friend,[41] who dispelled some of the confusion regarding relative humidity values. They stated that a relative humidity of 30 per cent may be effective where there is an excess of carbon dioxide and that a relative humidity of 65 per cent may fail to prevent the accumulation of static in the absence of carbon dioxide. The effect of increased atmospheric humidity in lowering the static danger by increasing the conductivity of the air would thus seem to depend on the electrolyte (chiefly carbon dioxide) content of the water vapor in the air. Others have attempted to correlate the efficacy of humidification with the voltage of the charge stored or dissipated.

Grounding or earthing has been and is employed by many anesthetists in an attempt to remove quickly any static electricity that may be discharged onto the patient, the operating table, or the anesthetic apparatus. Brown[29] advised, in 1924, grounding the cylinder or mask. Herb[4] recommended, in 1925, the use of a grounded conducting floor, to which all tables, stands, and apparatus are grounded. Livingstone[56] advised, in 1930, that the operating table and anesthetic apparatus be grounded; to make the apparatus entirely conductive she recommended the use of spiral wire around the breathing tubes and wire mesh around the breathing bag. Newcomer[32] recommended, in 1940, grounding of the patient, together with the use of intercoupling. Lewis and Boehm[57] stated, in 1925, that grounding the anesthetic apparatus, patient, anesthetist, and operating table would eliminate the danger of static spark. Phillips[17] felt that grounding increases the energy of a spark received from a visitor and heightens the danger of a short circuit to the patient; he stated that "the proper evidence on the whole is against the grounding method." Henderson,[13] in 1930, condemned the practice of grounding the anesthetic apparatus, maintaining that the protection was minimal and that the danger of short circuit from the electrical illuminating current was increased. Griffith[14] declared, in 1931, that grounding did not protect against static. Rovenstine,[37] in 1939, did not employ grounding. Waters' technique,[58] as described by him in 1943, did not include grounding. Draper[53] favored (1928) grounding all bodies in the danger zone.

Artificially ventilating the operating room has been recommended by several writers; Cheney,[59] in 1929, favored the use of a ventilating device to remove all escaping ethylene mixtures from the operating room. This practice probably owed its popularity largely to the high content of anesthetic gas in the operating room atmosphere before the widespread use of the carbon dioxide-absorption rebreathing technique, popularized by Waters. Phillips[17] recommended, in 1936, the use of ventilation. Newcomer[32] warned, in 1940, of the danger of air conditioning; this practice, he stated, removes from the operating room atmos-

phere much of the carbon dioxide, the electrolyte that plays a large part in making air conductive.

The electrically connecting together of the various parts of the surgery-anesthesia unit has been recommended by many investigators, on the basis that these separate components are thus joined to form one electrostatic body, so that static sparks cannot pass from one object or person to another so coupled.

Lewis and Boehm[57] stated, in 1925, that grounding the anesthetic apparatus, patient, anesthetist, and operating table would eliminate the danger of static spark. All individuals and objects concerned, therefore, were, in addition to being grounded, intercoupled, with a minimum of resistance. Herb[4] recommended, in 1925, the use of a grounded conducting floor, to which all tables, stands, and apparatus are connected; this, too, achieves direct intercoupling. Draper[53] also favored (1928) grounding all objects in the hazardous area, so as to include direct intercoupling. He used galvanized iron mats, that could be rolled up and were inexpensive; intercoupling was thus without high resistance and was associated with an attempt to render the anesthesia apparatus conductive by the use of wires inside the breathing tubes. Phillips[17] called attention, in 1936, to the danger associated with spiral wire used in tubing: the possibility of breaking of the wire with spark formation where the presence of an explosive mixture is very likely. Waters,[58] in 1943, did not include metallic intercoupling in his reported technique, but advised continuous contact between anesthetist and patient. Horton[55] advocated, in 1939, the use of intercoupling to reduce the hazard of explosion from electrostatic discharge. The chief objections to intercoupling were met by using conductors having high resistance. These objections were due to the increased hazard from electrical shock, in the case of an accidental connection between the patient and the lighting circuit, and the increased energy which would be associated with any electrostatic spark from a body not a part of the intercoupled system. A resistance of 100,000 ohms, he found, will limit the current resulting from contact with the lighting circuit to about 1 per cent of the amperage necessary to constitute a danger. "A conductor having a resistance of one megohm," he wrote, "will equalize any charge which might produce a sparking potential as rapidly as it can be established." Woodbridge, Horton, and Connell,[31] included in their published technique, in 1939, the use of resistance intercoupling, as did Wiggin[51] in 1940.

In 1941, Horton[21] again recommended the practice of high resistance intercoupling; he stated further, at this time, that grounding of the intercoupled system was beneficial. An estimate of the efficiency of the high resistance intercoupler in actual use was given by this author, who wrote, in 1941, the following: "Experience during the past year or more, in a large number of operating rooms, has disclosed nothing to indicate that the intercoupler fails to function exactly as intended. There have been no reports of discharges of sparks of the type it was designed to eliminate. There have been no reports of any fatal explosion during anesthesias protected by it. In fact, of 19 explosions during the 1939-1940 season, only one occurred in the presence of an intercoupler. This particular explosion is believed to have resulted from a spark of the type . . . against which the intercoupler is known to offer no protection." Referring again to the advisability of grounding the intercoupled group, he wrote: "As a more permanent and exclusive method of intercoupling, an electrically conductive floor is ideal." Many writers have indicated that the floor and the air are, if rendered conductive, universal intercouplers, equalizing potentials on all objects in contact with them. It has been shown, however, that even conductive rubber soles

become insulated after a few steps on a powdered surface. Horton[21] favored grounding the conductive floor, since, the object of intercoupling being the maintenance of everything in the room at one potential, and it being necessary that some objects be at ground potential, all objects should be at ground potential. He described four types of conductive flooring: (a) the embodying of metal strips in a terrazzo or tile floor; (b) conductive rubber flooring; (c) a laminated floor, consisting of a layer of thin porous tiles covering a thickness of cement, in whose upper surface a copper screen is incorporated; (d) calcium chloride treated tile or terrazzo floor. Sparks may be struck from tile, he pointed out, by iron or steel which may be present in shoes or metal furniture. Shoe soles of ordinary rubber, Horton stated, are dangerous; the resistance of leather may vary from 10,000 ohms to 10 megohms; conductive rubber is ideal for this purpose. Furniture in the operating room, he continued, should make contact with the floor through casters, feet, or crutch tips embodying conductive rubber or bronze (sparkless) drag chains. He wrote that surgeons' platforms, being insulators, are dangerous and should be coupled to the floor by feet of metal or conductive rubber. The patient should be directly connected to the table, for, as he warned, "in spite of all the conductive flooring and drag chains which may have been installed, the patient lying on the customary (operating table) pad is as completely isolated, electrically, as though he had been levitated." LeeRoy and Sword[1] suggested, in 1942, that charges may be built up too large for rapid dissipation to ground or intercoupled system, by the moving about in the operating room of charged bodies, and stressed the importance of the slogan: "Stand clear of anesthetic apparatus."

It is well known that substances differ widely in their ability to generate electrostatic charges. Horton[21] advised, in 1941, that removing a fabric case from a rubber pillow be prohibited in the operating room or in any room in which anesthesia apparatus is kept. The danger of static spark is due almost entirely, he wrote, to the presence of rubber and fabrics in the operating room. He recommended that the use of wool, silk, and silk substitutes (excepting undergarments) be prohibited. Rubber gloves and silk stockings, he felt, are not very dangerous as they maintain close contact with the body of the wearer. Woodbridge, Horton, and Connell[31] warned, in 1939, of the danger of having a cushion on the anesthetist's stool.

The use of conductive rubber throughout the anesthesia apparatus to render the machine conductive throughout, as well as on the furniture feet and shoe soles, has been recommended by many writers. Henderson[13] advocated the use of conductive rubber in 1930. Farrand[42] showed, in 1939, that the use of grounded conductive rubber prevented the accumulation of any readable potential on a breathing bag. Connell[50] felt, in 1939, that using conductive rubber would safeguard the apparatus as a generator of static spark. Newcomer[43] recommended, in 1940, the construction of a conductive rubber mat to be placed under the operating unit, the wearing of conductive rubber soles, and the use of conductive rubber in the anesthesia apparatus.

Wetting the various nonconductive or rubber parts of the anesthesia apparatus in an attempt to render them more conductive has been suggested by many authors. Connell[50] advised, in 1939, washing rubber tubes and bag with a calcium chloride solution to render the rubber conductive. Woodbridge, Horton, and Connell,[31] in 1939, suggested the value of wetting rubber parts before use. Horton[21] recommended, in 1941, rinsing all rubber parts used in anesthesia, with the exception of those touching the patient's or anesthetist's body, with a 2 per cent solution of calcium chloride.

Slocum and Finvold[60] stated, in 1944, that ionization of the air causes the atmosphere to become a low-grade conductor, with subsequent equalization of electrostatic charges on all objects within the area of ionization. They had determined that a minimum of 1,375 volts was required to explode a 25 per cent concentration of cyclopropane in oxygen; they set out to ionize the air to such an extent that the potentials of no bodies in the area concerned could differ by this amount. They investigated eight methods of ionizing air: (a) shielded open flame, (b) corona discharge, (c) ultraviolet light, (d) ion generator, (e) radioactive paint, (f) roentgen rays, (g) grenz rays, (h) radium emanations. Of these, the use of radium was the only method adaptable for use in the operating room which was safe and efficient. "At a distance of six feet," they wrote, "40 mc. of radon will decrease the static charges on all objects or persons to less than ignition potential within a few seconds. Working time of the operating room personnel who stay within a six-foot radius of 40 mc. of radon must be limited to eight hours." Woodbridge, Horton, and Connell[31] had previously warned (1939) that the production of ozone must be guarded against when the air in the operating room is being ionized, as both ozone-ethylene and ozone-cyclopropane mixtures are spontaneously combustible.

According to Greene,[9] ether-air is the only inflammable anesthetic that can be used safely in the absence of static precautions.

Several investigators have attempted to solve the problem of anesthetic explosions by avoiding the use of combustible mixtures. Nitrous oxide and pentothal, used separately or together, have been advocated by many as the drugs of choice in the presence of any obvious source of ignition. Greene[61] advised, in 1941, that only noncombustible anesthetic agents be used in the presence of x-ray apparatus. "Our study" (the committee appointed, in 1937, by the American Society of Anesthetists to study the problem of anesthetic fires and explosions), he wrote again[9] in 1941, "forces us to conclude with the bold statement: anesthetic fires and explosions ignited by diathermy, like those due to x-ray apparatus, are completely preventable only by the use of noncombustible anesthetic methods."

Attempts have been made by several writers to create mixtures of combustible gases, particularly cyclopropane, rich enough in cyclopropane and oxygen to be anesthetically potent and safe, yet rendered noncombustible by the addition of other gases. Jones, Kennedy, and Thomas[62] found (1940) that dilution with inert gases had little effect on the lower limits of inflammability of cyclopropane in air or in oxygen, but had a marked effect on the upper limit. Three inert gases were tested: carbon dioxide, helium, and nitrogen. Carbon dioxide proved to be the most efficient flame quencher, but is physiologically too active to be used for this purpose. The flame quenching properties of nitrogen and helium are about the same. The flame quenching property of a gas, they stated, depends on its molecular heat capacity and on its thermal conductivity; helium's heat capacity is low, but its thermal conductivity is very high. It can be breathed with less effort than nitrogen, they pointed out, a distinct advantage when the oxygen content is lowered. According to Coward, Cooper, and Jacobs,[77] they stated, another advantage of using helium is the fact that mixtures of gases in which helium is present cannot be as easily ignited by electric discharge as can mixtures containing the same concentrations of other inert gases. While potent noninflammable mixtures can be thus created, they warned that adding air or oxygen would make them explosive, and that a leak might thus cause a combustion; the violently explosive mixtures, however, are avoided.

Jones and Thomas[63] offered, in 1941, a technique of administering anesthesia with such noncombustible cyclopropane-oxygen-helium mixtures. They stressed the importance of not flushing the patient with oxygen at the end of anesthesia, because of the danger of returning the mixture into the explosive range. It seems, however, that breathing room air would tend to achieve the same result. Griffith[14] advised, in 1931, that carbon dioxide, being a fire extinguisher, be used to flush out all gas machines after use. Jones and Thomas[63] admitted certain difficulties encountered in their attempt to eliminate the explosive hazard by diluting the mixture with an inert gas, due to (a) the variable oxygen needs of different individuals, (b) the sudden change in all concentrations attending a leak, and (c) the difficulty attending the determining of the concentrations of oxygen in the apparatus. Writing in 1943, these same authors[64] maintained that the practice of adding nitrous oxide to ether-oxygen mixtures, in an attempt to render the mixture noncombustible, is harmful rather than advantageous, since, as they showed, the lower limit of inflammability of ether in oxygen is further lowered by the addition of nitrous oxide. They were unable to find, during the course of further experiments, any ether-nitrous oxide-oxygen mixtures that were both noninflammable and suitable for anesthetic purposes. Clinical experiments, in which samples of ether-nitrous oxide-oxygen mixtures being given by different anesthetists were tested, showed that almost all mixtures used were explosive. The addition of helium, they stated, is of no value in eliminating the explosive hazard of these mixtures. The explosiveness of ether-oxygen mixtures and the danger involved in adding nitrous oxide to ether-air and ether-oxygen mixtures were mentioned in an editorial of the *British Medical Journal* in 1936.[65] Haas, Hibshman, and Romberger[66] were able, in 1940, to produce cyclopropane mixtures that were nonexplosive and anesthetically potent, by adding air to cyclopropane-oxygen mixtures. The mixtures they arrived at were similar to those tested by Jones, Kennedy, and Thomas,[62] who diluted cyclopropane-oxygen mixtures with helium; Haas and his colleagues used nitrogen instead of helium, and were able to do this by simply adding room air to the breathing bag by means of an attached bulb. They showed, by means of a flammability graph, that all such mixtures were nonexplosive if they contained no more than 20 per cent of cyclopropane or no more than 11½ per cent of oxygen; the graph showed, however, that mixtures richer in both cyclopropane and oxygen could be used without danger of explosion. Means of accurately creating such mixtures and devices for rapid analysis of the mixtures seemed to be desirable. Horton[67] stated, in 1941, that adding an inert gas or even an explosive gas to a mixture of another explosive gas and oxygen may result in a mixture that is anesthetic, nonexplosive, and with a sufficiently high oxygen content. He cited two mixtures: the first containing 20 per cent cyclopropane, 50 per cent ethylene, and 30 per cent oxygen, for deep anesthesia; the second containing 10 per cent cyclopropane, 65 per cent ethylene, and 25 per cent oxygen, for light anesthesia; in either of these mixtures is the dilution obtained by the use of an inert gas. Cooper[39] stated, in 1939, that oxygen concentrations must be reduced below 10 per cent to prevent explosions, so that the addition of inert gases to explosive mixtures to reduce the oxygen concentration to a point where explosions cannot occur would not be practicable. Greene,[9] in 1941, drew attention to his being unable to find any static explosion of cyclopropane-air; there were two explosions, however, of cyclopropane-oxygen-helium mixtures. Lee-Roy and Sword,[1] in 1942, decried the practice of diluting the anesthetic gas mixture with inert gases; they considered it difficult to estimate the amounts of

anesthetic agent, oxygen, and inert gases to maintain a proper degree of narcosis, avoid hypoxia, and secure a nonexplosive mixture. Greene[25] spoke, in 1942, of the "relative harmlessness which is associated with the combustion of any anesthetic mixed with air."

At least one attempt has been made to protect the patient by shielding him from the explosion that may occur despite attention to ignition and to the inflammability of the mixture. Hornor and Gardinier,[68] working with ethylene (1928), were able to intercept explosions experimentally. They constructed a mask incorporating a cylinder containing (a) fine mesh screen wire, (b) a by-pass, and (c) a valve which was closed, automatically, by the force of the explosion, in about $\frac{1}{5000}$ of a second; they estimated the maximum rate of propagation of ethylene-oxygen explosions to be 2,500 meters or 1½ miles per second. This device, obviously, could protect the patient only from an explosion originating in the machine.

Salzer[69] described, in 1927, a method of removing spent ethylene-oxygen mixtures from the operating room. Cheney,[59] in 1929, advocated the use of copper screens to prevent the propagation of ethylene explosions and the use of a ventilating device to remove all escaping ethylene mixtures from the operating room. The closed rebreathing technique, popularized by Waters, has, of course, done much to eliminate the possibility of escape of large amounts of explosive mixtures.

The matter of leaks has received considerable attention. Brown[29] stated, in 1924, that the possibility of explosion when ethylene was allowed to escape was "only in the remote realms of possibility." Tyler, in discussing an article by Woodbridge, Horton, and Connell,[31] in 1939, attributed to Connell the statement that diffusion is so great that cyclopropane leaking at a rate of 4 L. a minute will not explode four or five inches from the leak. Connell asserted,[50] in 1939, that gas diffusion is sufficiently rapid to render difficult, experimentally, flash backs from open flame six inches from the spillway; in the case of liquid ether, however, flash backs can occur from several feet away. Knight[70] has been unable to obtain an explosive mixture at a distance of two inches from an open leak of 500 c.c. per minute of a known explosive mixture of cyclopropane-oxygen. Greene[9] collected 10 cases in which ether, ethylene, and cyclopropane have been ignited more than twelve inches from the nearest leak, but could find no fatality caused by the presence of cautery or flame outside a twelve-inch radius surrounding the upper respiratory tract. In reviewing 57 fires and explosions caused by flame or cautery, he wrote, "all deaths—and all were patients—have been the result of a flame or cautery employed within a twelve-inch danger zone surrounding the upper respiratory tract." "Dr. Squibb," McCardie wrote,[71] "has seen ether take fire at a measured distance of fifteen feet between the source of escaping vapour and the source of fire"; the direction of escaping vapor was not mentioned. Leaks of ethylene have inspired many comments on the fate of this gas, whose density approximates that of air, in the operating room atmosphere. Rovenstine[37] has quoted Waters to the effect that ethylene floats in strata, and that static explosions always occurred within the apparatus, not without. Guedel,[18] Davis,[72] and Sise[46] believed, too, that ethylene can float in combustible layers in an operating room. Brown,[29] Jones,[73] and Phillips[17] stated, however, that ethylene diffuses rapidly because of its lightness, to subexplosive levels.

Wineland and Waters[74] showed that true diffusion of gases takes place through intact rubber. Ten liter bags filled with various gases lost, in forty-

eight hours, the following weights, approximately: oxygen, 0.32 Gm.; ethylene, 1.00 Gm.; carbon dioxide, 4.68 Gm.; nitrous oxide, 7.00 Gm. Starting weights, apparently inclusive of the bags, ranged from about 112 to 192 Gm. The diffusion into the bags of the various components of the room air does not seem to have been considered, despite the fact that on one occasion, one of the bags gained in weight; the order of diffusion rates would not appear to be affected, however, these rates do not seem great enough to contribute to the danger of explosion. Flagg,[75] in 1937, recommended the practice of aspirating, into a small rubber syringe, the atmosphere overlying the operative field where the cautery is to be used; the contents of the syringe are then blown into the flame of an alcohol lamp. The cautery is believed to be safe if no change occurs in the color of the flame.

That explosions can occur without ignition has long been recognized. Greene[9] divided the cases of fire and explosion, due to the high pressure under which anesthetic gases are stored, into three groups: (a) the sudden release of pressure into insufficiently protected parts of the apparatus; (b) "the passage of oxygen at high speed over combustible material, such as oil or a leather washer"; (c) mixing nitrous oxide and ethylene under pressure. Spontaneously combustible ozone mixtures have been mentioned. Sise[46] stated that a mixture of ethylene and oxygen at high pressure may explode spontaneously.

The inflammability of the patient's breath has been discussed by many writers. Pinson asserted,[10] in 1930, that air exhaled two or three minutes after the termination of an ether anesthesia contains too little ether vapor to ignite. Williams,[12] in 1930, and Livingstone and co-workers,[8] in 1939, warned that the patient's breath may remain explosive for some time following an anesthesia, so that precautions even on return to the room or ward would be necessary. Guedel[18] maintained, in 1937, that the breath is noninflammable six or eight minutes after the termination of cyclopropane anesthesia; Connell[50] stated, in 1939, that the patient's lungs and the gas apparatus can be made free of ignitable gas in approximately two minutes by using a high flow of a noncombustible mixture and emptying the breathing bag several times.

Although the closed, rebreathing technique has done much to lower the explosion hazard, Greene[9] collected reports of 18 explosions occurring during anesthesia administered by this method; these were attributed to breaking the circuit, favoring static spark formation and liberation of an inflammable mixture.

WHAT IS BEING DONE?

The role of the manufacturer of anesthesia apparatus includes, according to Connell,[50] the reduction of the possibility of ignition from mixture of combustible gases under high compression by furnishing an individual reducing valve for each cylinder, the use of nonsparking metals, gas-tight connections, and the construction of a central spill valve (to direct the flow of discarded gases away from the operating table and electrical equipment).

Precautions to be taken by the anesthetist would include: (a) the avoidance of combustible agents in the presence of obvious hazards, such as the cautery;[9, 17] (b) eliminating the practice of washing out patient and apparatus with oxygen following an anesthesia;[12, 13, 76] (c) the use of caution in spilling gas; (d) the employment of the intercoupler[21, 32, 51, 55, 57] or the maintaining of continuous contact by the anesthetist with patient and machine[58]; (e) use of the rebreathing technique[58]; (f) washing tubes, bags, and mask with water or

calcium chloride solution;[21, 31, 50] (g) elimination of unnecessary, sudden movements by the anesthetist, and of unnecessary adjustments of the mask.

The duties of the hospital have been stated by various writers to include: (a) the installation of safe lights, switches, and electrical wiring (the three-wire system); (b) the maintenance of a high humidity in the operating room;[13, 14, 37, 39, 47, 51] (c) the prohibition of wool, silk, and ordinary rubber; (d) the banning of visitors from the area surrounding the anesthetic apparatus[1]; (e) banning of open flame, cigarettes, etc., from the operating room; and (f) the construction of a grounded, conductive floor.[4, 21]

The following is a list of some of the devices and practices recommended in the articles reviewed.

1. Safety wiring (three-wire type)[41]
2. Switches
   (a) mercury (vaporproof)[16]
   (b) same, with pilot light
   (c) outside operating room[16]
3. Elevated electric outlets
4. Grounding[32, 56, 57]
5. Intercoupling
   (a) complete[46, 47, 57]
   (b) resistance[21, 31, 41, 55]
6. Ventilation
   (a) alone[59]
   (b) with humidification[14]
7. Wire screens
8. Humidification[13, 14, 17, 31, 37, 39, 47, 48, 51-54]
9. Banning of wool and silk[21]
10. Sparkproof motors[9]
11. Grounded floor plate[16, 53]
12. Conductive flooring[16, 21, 32, 41]
13. Conductive rubber[41, 43]
14. Dilution of mixture
    (a) with inert gas[62, 63]
    (b) with inflammable gas[67]
15. Nonsparking metals[21, 50]
16. Elimination of flame, cautery, smoking, x-ray, faulty instruments, etc., in the presence of a combustible gas[9, 13]
17. Alertness[9]
18. Rebreathing technique[8, 17, 31, 41, 70]
19. Intercepting valve[68]
20. Keeping visitors away from apparatus[1]
21. Large rooms, to prevent brushing of people against equipment and each other
22. Continuous contact with hand and mask before beginning and during anesthesia[8, 58, 70]
23. Banning of ordinary rubber soles and metal shoe spikes[21]
24. Ionization of air[60]
25. Rinsing tubes and mask
    (a) with water[31, 70]
    (b) with calcium chloride solution[32]

26. Washing floor with calcium chloride solution[32]
27. Eliminating ordinary rubber in the operating room[21]
28. Washing out machine with carbon dioxide at end of anesthesia[14]
29. Wet flowmeters
30. Turning on cylinder valves slowly[48]
31. Blowing off some oxygen when starting a new cylinder[48]
32. Keeping nitrous oxide and ethylene on separate machines,[56] or if on same machine, never opening both cylinders at one time[18]
33. Avoidance of unnecessary movements by the anesthetist and of frequent adjustments of the mask
34. Endotracheal technique[70]

WHAT DOES THE FUTURE HOLD?

Griffith[14] cited, in 1931, Henderson's statement to the effect that the discovery of any new nonexplosive gases was unlikely, and that the solution lay in humidification rather than in a search for a noncombustible anesthetic gas. Jones and Thomas,[63] in 1941, expressed their belief that the solution to the explosion problem in anesthesia lies in avoiding the use of explosive mixtures, that "mixtures containing 20 per cent cyclopropane and 80 per cent oxygen, now commonly employed, are so violently explosive that their use should be discouraged."

It is significant that, despite the numerous precautions recommended and undoubtedly practiced in connection with the problems of explosions in anesthesia, Haas, Hibshman, and Romberger[66] could state, in 1940, that "there has been no apparent decrease in the number of explosions."

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CYCLOPROPANE—A PERSONAL EVALUATION

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I ANESTHETIZED the first patient with cyclopropane on Oct. 9, 1930. From then until Sept. 1, 1944, this gas has been used as the major agent to anesthetize about 25,000 patients at Wisconsin General Hospital. It has been used as the induction agent and as an adjuvant in many additional administrations. For all these, I have been personally responsible, although actual administration has been conducted by others of skills varying from that of the fourth-year medical student to that of my associates with years of experience in clinical anesthesia. My confreres in the departments of surgery, pharmacology, and physiology as well as in the department of anesthesia have cooperated in the study and evaluation of the advantages and disadvantages of this agent. Their experimental findings, clinical impressions, statistical evaluations, and personal conclusions as well as my own have been published at various times.[1-30]

I shall attempt to state my present personal impressions as to the value of cyclopropane in the anesthetist's armamentarium. This opinion will be based largely upon personal experience in the operating rooms, influenced by the experimental findings at the University of Wisconsin and elsewhere when these have been verified by clinical observation. A regrettable repetition of personal pronouns seems necessary in such a discussion. It will be taken for granted that the reader is familiar with our former publications and therefore only those present opinions will be emphasized which are at variance with those previously expressed.

Received for publication, Oct. 2, 1944.

POTENCY

Dosage, Concentration, Premedication.—Some of our former publications failed to give proper weight to an earlier finding; namely, that previous administration of morphine to dogs reduced by 12 per cent the concentration of cyclopropane required to produce a given amount of depression.[3] The administration of morphine, barbituric acid derivatives, scopolamine, and atropine to normal persons convinced us that adequate "drying" and sedative effects could be secured with much smaller doses of these agents before anesthesia than we had been using.[31-33] With markedly less premedication (one-quarter to one-half the doses formerly used) higher concentrations of cyclopropane can be employed without encountering too great depression of respiration. The importance of this fact will appear later. The extreme potency of cyclopropane, plus the rapidity with which the concentration of such a gas can be built up in the blood and tissues,[4] increases the technical danger of "overrunning" the dosage past the optimum point of effect for satisfactory anesthesia and into the realm where essential physiologic functions (such as respiration) are depressed or abolished. Obviously, adequate ventilation of the alveolar spaces is essential if control of saturation and desaturation of the tissues is to be maintained.

Respiration and Abdominal Relaxation.—Certain muscles of the abdominal wall are, at least accessory, muscles of respiration. Fortunately, the function of breathing resists depression by anesthetic drugs. Otherwise embarrassment to the anesthetist during their administration would be even more frequent than it is. In another sense, however, this is unfortunate because the margin between flaccid relaxation during operations in the upper abdomen and total paralysis of all the muscles of respiration is very narrow. Many of the older inhalation agents in moderate dosage tend to increase the activity of the muscles of respiration. Cyclopropane lacks this quality. Hence, in the case of cyclopropane, the margin between the point of partial paralysis of respiratory muscles necessary for relaxation of the upper abdomen and respiratory arrest is narrower. Dosage of cyclopropane must, therefore, be increased with the greatest care in the approach to relaxation of the upper abdomen lest the desired concentration be exceeded, resulting in ventilation which is inadequate to produce further saturation or to maintain the relaxation that has already been secured. Obviously previous depression of respiration by other agents is undesirable. If the anesthetist does not possess the necessary patience, skill, and mechanical equipment to accomplish a gradual saturation to the point of adequate relaxation without too much effect on respiration, he must resort to other means. Either he must supplement the administration with another agent, as for example ether or procaine, or he must resort to the use of artificial means of ventilating the lungs, abandoning dependence upon natural breathing for the time being. The latter course (the control of respiration by the anesthetist) has, in my estimation unfortunately, come to be utilized all too frequently. It is true that relaxation can thus be improved. Controlled respiration has the further advantage of placing movements of the diaphragm and the lungs under the control of the anesthetist. He may then in certain cases coordinate these movements with the steps in technique of certain operations (for example, on the lung or diaphragm) in a manner to simplify the surgeon's work. In such cases, controlled respiration is amply justifiable. Artificial ventilation is always better than inadequate natural breathing. However, if I am forced to use controlled respiration with cyclopropane solely for

the purpose of securing proper muscular relaxation, I do so with an admission that I have failed in patience, skill, or mechanical control in the technique used. "Good anesthesia" ought not to deprive a patient of so essential a function without a very good reason.

EFFECTS ON THE CIRCULATORY SYSTEM

A decrease of pulse rate from 120 beats per minute to 70 was observed when cyclopropane was administered to the first patient in 1930. The rate returned to 120 after the cyclopropane had been discontinued. In nearly all the patients skillfully and deeply anesthetized since then, the pulse rate has been between 60 and 70. During our early studies, intentional overdose sufficient to stop respiration, was administered to both dogs and patients on a good many occasions. Although arrhythmia was produced on some occasions, the appearance of these animals and patients was rarely alarming. Two series of comparative electrocardiographic studies were then initiated,[3, 7] one with dogs and one with patients. In order to eliminate the effect of inadequate ventilation (excess of carbon dioxide and deficiency of oxygen), controlled respiration was instituted in all these studies before doses had been reached which would decrease ventilation. Individual variability was found but the fact was established that a direct relation exists between the concentration of cyclopropane and the occurrence of arrhythmia. It was also established that the effects on cardiac rhythm are usually reversible as soon as the concentration in the tissues is decreased. These conclusions persist after reconsideration forced upon us by statements of other workers. Suggestions that adjuvant medication (ether, barbituric acid derivatives, procaine, etc.)[19, 20, 34-36] or further saturation with cyclopropane[37] are proper practical means of eliminating arrhythmia have *not* received support from my clinical observation. It seems safer and wiser to avoid arrhythmia when possible by using a conservative approach to the lowest effective concentration and to treat arrhythmia, when it occurs, by prompt reduction in the concentration employed. We continue to use scopolamine but in smaller doses than formerly and for a different purpose. It may or may not provide some protection against arrhythmia.

The question arises as to whether cyclopropane should be administered to patients suffering from diseases of the circulatory system. Such patients tolerate poorly physiologic insult of any sort. The abnormal pressure relations created by respiratory obstruction, the effects of lack of oxygen, of extreme changes of position, of loss of fluid, and all the other hazards of operation and anesthesia are exaggerated in the presence of cardiac disease. Protection from errors of technique is doubly important for such patients whatever the agent used. I personally have not avoided the use of cyclopropane in the presence of circulatory disease. The clinical impression gained has been that such patients are not more susceptible to specific damage from the effect of this drug than are other patients with normal circulatory systems.

AUTONOMIC EFFECTS

Considerable evidence has accumulated in support of the belief that cyclopropane hyperactivates certain of the autonomic mechanisms.[38, 39] Bronchial constriction has been observed. Certain occurrences during cyclopropane anesthesia have been explained as due to an oversensitive sinoaortic or vagal mechanism which has even caused cessation of breathing and of the heartbeat. Considerable thought has been devoted to an analysis of our own clinical ex-

perience in this regard. After eliminating the effects of medication with other drugs (opiates, barbiturates, and the atropine group), our present opinion is that variable hyperactivation of the autonomic reflexes may occur in some individuals during insufficiently profound anesthesia with cyclopropane and intensified by the agent. From a practical standpoint, three methods seem to have been useful for the prevention of such reactions:

1. Premedication with scopolamine or atropine. Scopolamine in moderate doses, I think, has been reasonably effective.

2. The administration of nitrous oxide anesthesia as an accompaniment of cyclopropane has appeared to have prophylactic value. When such a reflex has been elicited, a short period of reversion to nitrous oxide has on certain occasions seemed to relieve the condition, permitting a later return to cyclopropane anesthesia.

3. Rapid induction with nitrous oxide-oxygen and cyclopropane to second plane anesthesia in preference to a slow induction with cyclopropane in oxygen as a vehicle has seemed to decrease the occurrence of such reflexes. Hypoxia should, of course, be scrupulously avoided. If one can anticipate the application of a stimulus to such deep reflexes as those originating in the mediastinum or upper abdomen, I believe that he can produce profound enough anesthesia with cyclopropane to prevent the embarrassment.

THE RESPIRED ATMOSPHERE

Experience of many years in the administration of agents by inhalation supports the following general principle. For "normal" persons, the concentration of oxygen in the anesthetic atmosphere should resemble that to which they are accustomed. When the mechanism of the patient for the transport of oxygen is defective, excess of oxygen should be limited to that which will compensate adequately for the deficiency in transport. Any great excess of oxygen over the 20 per cent normally available tends to permit us to overlook inadequate ventilation. Such an excess interferes with transport of carbon dioxide and a "pink" patient may suffer from considerable physiologic embarrassment. The tendency to disturbance of acid-base balance in modern anesthesia is often due to attempts to keep a patient pink with added oxygen in the presence of depressed or obstructed breathing. Maintenance of atmospheres during anesthesia, at or near the normal content of oxygen, will help to prevent this mistake. Inadequate exchange or obstruction will thus result in the warnings (for example, changes in pulse rate, blood pressure, breathing, color, etc.), and the condition will more likely be corrected. Of course, if depression or obstruction of respiration cannot be remedied, atmosphere enriched with oxygen is preferable to persistent hypoxia. Such a procedure, however, often corrects only a part of the abnormality. When considerable enrichment of the respired atmosphere with oxygen has been deemed necessary during anesthesia, it has proved helpful to reduce the oxygen gradually as the end of operation approaches so that the reaction of the patient may be observed.

Carbon Dioxide Absorption Technique.—Since cyclopropane does not increase respiratory exchange, the importance of properly adjusted absorption technique is easily neglected. Saturated soda lime, excessive dead space between the patient and the soda lime and excessive depression with nonvolatile drugs are all dangers which, if overlooked, may result in serious physiologic disturbance. Unless the administrator is familiar with the physiologic basis of anesthesia, he will do well to use a technique other than carbon dioxide ab-

sorption and an agent other than cyclopropane. It ought always to be kept in mind that anesthetic apparatus, including that designed for carbon dioxide absorption, has usually been devised for use with normal adult individuals. In dealing with the very weak and ill and particularly when anesthetizing children, the dangers of this technique are intensified. Unless specially arranged equipment can be used in such cases, cyclopropane had better be administered by an open method if at all.

Effects of Hot Weather.—Since no new facts have been determined since our earlier reports, it remains important to appreciate the dangers inherent in the accumulation of heat and moisture in the closed atmosphere. The changes resulting, perhaps from one of these factors, appear to hypersensitize the patient to the effects of accumulated carbon dioxide. Contrary to the belief of some anesthetists, absorption technique rarely accomplishes complete removal of carbon dioxide from the inspired atmosphere. When anesthetizing a patient suffering from fever on a hot day, the slightest muscular twitching or other abnormality should be sufficient reason for abandoning "carbon dioxide absorption."

The Hazard of Fire and Explosion.—Not only does the use of excessive percentages of oxygen predispose to the occurrence of unphysiologic conditions, but it also produces an atmosphere which can be ignited with less heat. Although judicious use of absorption technique should eliminate the fire hazard, whatever the atmosphere contains, the less explosive the mixture the better. In the 25,000 administrations mentioned, ignition of cyclopropane has taken place only once when a bag and canister containing oxygen and cyclopropane were carelessly dropped to the floor.[30]

SUMMARY

1. The relation of the potency of cyclopropane to the use of opiates, barbiturates, and atropine-like drugs has been discussed. Necessity for limiting the dose of agents which depress respiration in conjunction with cyclopropane has been stressed. The narrow margin between relaxation of the muscles of the upper abdominal wall and those of respiration has been mentioned.

2. The importance of skillful slow approach to maximum saturation when arriving at profound anesthesia for upper abdominal operations has been emphasized. If this fails, personal preference has been expressed for supplementation with intercostal block anesthesia, curare, or some other method rather than resorting to "controlled respiration" for the sole purpose of producing more profound anesthesia. Controlled respiration should, in my estimation, be reserved for occasions when such control, synchronized with the surgeon's maneuvers, facilitates operative technique. Resort to it will probably continue to be a temporary solution of unexpectedly difficult situations.

3. A decrease in pulse rate to between 60 and 70 has, in my hands, been the usual accompaniment of well-conducted cyclopropane anesthesia. A marked and sudden decrease from this rate to below 50 has been observed to precede a sudden tachycardia. Arrhythmia may be seen before, during, or after these changes. When marked bradycardia, tachycardia, or arrhythmia occurs, a circulatory emergency is present and instant rapid desaturation should be begun, by artificial respiration if necessary. Dependence upon the prophylactic value of adjuvants (ether, barbiturates, atropine, etc.) or the therapeutic value of increasing saturation with cyclopropane appears, in my experience, to be unreliable and dangerous.

4. During very light cyclopropane anesthesia, the autonomic reflexes in certain individuals are hyperactive. Rapid induction to second plane anesthesia and the use of nitrous oxide as a vehicle during induction have seemed to reduce the frequency of adduction of the vocal cords. Reflexes induced by surgical trauma can usually be prevented by sufficiently profound anesthesia when produced before the stimulus is applied. However, exceptions have been observed. Scopolamine and atropine and perhaps nitrous oxide may be useful prophylactically.

5. It has been suggested that anesthetic atmospheres should, as nearly as possible, resemble normal atmospheres. Substitutions should be made with the welfare of the patient in view and then only sufficient change ought to be made to accomplish the desired effect. If technical facility and familiarity with the signs of hypoxia are lacking, oxygen as a vehicle is safer.

6. Certain dangers inherent in the use of the carbon dioxide absorption technique have been pointed out.

7. My experience of nearly fifteen years with cyclopropane leaves me with the personal impression that this agent permits rapidity of control of the depth of anesthesia impossible with other inhalation agents. However, this very fact may result in unfortunate and disastrous results when ignorance or carelessness accompany the administration.

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PROLONGED ANESTHESIA

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AT THE University of Minnesota Hospitals, due to the established ways of referring patients to the hospitals and to the staff, and due to the system of selection of admissions, it has come about that a larger than average number of complicated or long surgical procedures are carried out. It is perhaps of interest to report 1,000 consecutive operations which required anesthesia of three hours' or more duration.

In June, 1942, Grimm[1] reported to the staff 454 such consecutive cases ending April 27, 1942, and one year later Smith[2] reported an additional 385 such cases in the following twelve months ending April 27, 1943. In this communication we have added the succeeding 161 cases to complete the 1,000 and have consolidated them. In Table I we have shown the number of each of the main groups of cases, the average ages in each group, and the average durations of anesthesia in each.

TABLE I

	AVERAGE AGE (YR.)	NUMBER OF CASES	AVERAGE DURATION HR.	MIN.
Brain	39	129	4	33
Other neurosurgery	40	79	3	35
Chest	25	33	5	13
Gastrectomies	57	308	4	45
Other gastrointestinal	54	256	4	14
Miscellaneous	46	195	3	37
Total		1,000		

Table II shows the preoperative conditions of the patients and indicates to a large extent how well the patients are prepared for surgery. The figures of the three different collections are remarkably uniform but show a tendency toward an increase in the preoperative hemoglobin and plasma protein in all but the chest cases, in which there has been a decrease.

TABLE II. PREOPERATIVE CONDITIONS OF PATIENTS

	AGE (YR.)	PREOP. BLOOD PRESSURE SYST.	DIAST.	HB. (GM.)	PLASMA PROTEIN (GM.)
Brain	39	168	78	13.16	6.35
Other neurosurgery	40	149	73	13.50	6.70
Chest	25	134	75	11.60	7.10
Gastrectomies	57	132	75	13.90	6.70
Other gastrointestinal	54	132	71	12.00	6.90
Miscellaneous	46	136	76	12.90	6.50

Table III shows the preoperative medication. Barbiturates were practically not used at all. In the first series of 454 cases more patients in each classification received codeine than morphine. About five years ago one or two of the surgical staff had had some bad results which were ascribed to

Received for publication, March 12, 1945.

morphine so that morphine was interdicted in all brain cases, in all chest cases, and for all patients over 50 years of age. We still give no morphine in brain cases but other patients receive it in proportion to our judgment of their vigor, etc. Some who received codeine were so evidently undermedicated that they were also given morphine intravenously upon arrival in the operating room. In the earlier survey 60 per cent received atropine and 40 per cent received scopolamine. Since then almost 100 per cent have been given scopolamine, and we believe that it adds to the "don't care" composure of the patient and is more efficient in controlling secretions.

TABLE III. PREMEDICATION

	MORPHINE	CODEINE	ATROPINE	SCOPOLAMINE	BARBITURATE
Brain	12	108	47	81	1
Other neurosurgery	43	30	11	59	
Chest	12	20	12	21	
Gastrectomies	304	79	73	204	
Other gastrointestinal	183	70	74	178	
Miscellaneous	166	15	32	160	6
Total	720	322	249	703	7

Table IV shows the anesthetic agents used. During the whole series the customs in anesthesia have remained much the same except that cyclopropane definitely increased, ethylene definitely decreased, and spinal anesthesia became much more largely used for the long abdominal operations. In the first series only 6 spinal anesthesias were given to the 155 patients with gastrectomies and 7 were given to the patients in the 127 other gastrointestinal cases. In the following 153 gastrectomies, 143 spinal anesthesias were given, and in the following 129 other gastrointestinal cases 109 spinal anesthesias were given. The first spinal anesthesias for these long operations were administered by the continuous technique but certain occasional inconveniences influenced us to change to the much longer lasting spinal anesthetic drug, nupercaine, with the single injection method. This provides spinal anesthesia for three hours or longer.

TABLE IV. ANESTHETIC AGENTS

	CYCLOPROPANE	ETHYLENE	ETHER	PENTOTHAL	SPINAL	CURARE	TRACHEAL TUBE NO.	TRACHEAL TUBE (%)	LOCAL
Brain	102	18	6	7	0	0	119	92	0
Other neurosurgery	77	2	2	1	0	0	72	91	0
Chest	26	2	0	7	0	0	26	78	0
Gastrectomies	297	44	4	12	149	2	289	93	0
Other gastrointestinal	248	32	3	12	116	4	207	81	0
Miscellaneous	131	34	27	36	18	0	73	37	6
Total	881	132	42	75	283	6	786	78	6

It is most interesting to look back and consider the development of our anesthesia for the major abdominal surgery. Up to twenty years ago, the anesthesia was all drop ether. We considered then that any abdominal procedure requiring more than three hours carried more than a 50 per cent risk from both the anesthetic and surgical standpoint. While we used nitrous oxide with ether in some cases, we did not consider it much of an improvement. Twenty years ago we began to use ethylene, almost always with ether, and soon began to feel that a definite improvement had been made.

In the fall of 1933 we began to use cyclopropane but not until 1935 did we use it for major upper abdominal surgery and found that in nearly 50 per

cent of cholecystectomies, for example, we were obliged to add ether to the cyclopropane in order to obtain satisfactory relaxation. Our technique in the use of cyclopropane improved until by January, 1939, when the presently reported series of long surgical procedures began, we practically never found it necessary to use any ether. However, we have always been, and still are, required to produce cadaverous relaxation and almost unnoticeable breathing to expedite the surgical procedure. This we accomplished by employing a sufficient concentration of cyclopropane and by carrying on artificial or "controlled" respiration by manual manipulation of the breathing bag. It is interesting that of the 149 gastrectomies and 120 other gastrointestinal cases in this series, averaging five hours six minutes and four hours six minutes, respectively, before we had begun to use any spinal anesthesias for such cases, only two patients with gastrectomies and two patients in other gastrointestinal cases received any ether. We observed that the operative and postoperative course and recovery time of these patients were better than with any preceding type of anesthesia.

It was in April, 1942, that we began to extend our use of spinal anesthesia from the shorter abdominal operations to those which we were quite sure would require three hours or more of anesthesia. In all of such cases we have consistently induced general anesthesia as soon as the spinal anesthesia has been induced and confirmed. We do not believe it is necessary or helpful to submit the patient, in long procedures, to the weariness of lying awake even a part of the time. Besides, the manipulations necessary in any upper abdominal operations and bowel resections usually cause nausea and retching under spinal anesthesia alone, which is miserable for the patient and disturbing to the surgeon. The purpose of the spinal anesthesia is to spare the patient the prostrating effect of long, deep general anesthesia, and therefore we took pains to keep the level of general anesthesia in the first plane of the surgical stage as long as the spinal anesthesia remained effective. As the latter faded out, we deepened the narcosis as much as required to afford relaxation. Throughout both phases of the anesthesia we exercised controlled respiration as much as necessary to effect quiet respiratory movement. We were impressed by the fact that these patients who had been given spinal anesthesia looked even better postoperatively, had even less prostration, and recovered their vigor even more rapidly than those who had been anesthetized by cyclopropane alone.

It will be noted in Table IV that only 6 of the patients in the 1,000 long operations in this series received curare. The end of this particular series marks the beginning of our use of curare in such cases. We added curare to our armamentarium in May, 1943, and for several months used it only for abdominal operations lasting up to two hours. After thus becoming well acquainted with it, we began to use it in the long procedures at the dwindling of the spinal anesthesia relaxation, thus avoiding the deepening of the general anesthesia. These six cases represent the beginning of this further evolution and they were pleasing enough to encourage us to continue. Discussion of this experience, of course, goes beyond this presently reported series of 1,000 long operations, and will be reported in a later series. It should be said here, however, that, because of the occasional postspinal anesthesia headache and possibly a higher incidence of catheterization after spinal anesthesia, after a few months' trial of curare for prolongation of the relaxation, we began to substitute it for spinal anesthesia in our long procedures from the beginning. It has seemed that this has helped to bring about a still further gain in the

rapid return of vigor. As one surgeon expressed it, "These patients with 75 per cent or more gastrectomy now cannot see why they should not go home on the fourth postoperative day." They do average only seven and a fraction postoperative days in the hospital.

It must be emphasized, of course, that in addition to improved anesthesia, they receive excellent preoperative preparation and are given adequate operative and postoperative fluids, plasma, blood, and vitamins.

The twenty-four pentothals for gastrointestinal patients were all for induction only, and the tendency toward this use of it has increased largely in later cases.

It will be noted that of 129 cases of brain surgery, 102 patients received cyclopropane, 18 ethylene, 6 ether, and 7 pentothal. The last were for induction only, the ethers were for children, and the ethylenes were in some of the earlier cases, and some in which it was combined with cyclopropane. Cyclopropane is our standard method. In years past we used open ether, rectal ether, rectal avertin, and either of these supplemented with chloroform. We believed that any gas anesthetic was contraindicated because of increased intracranial pressure. The intratracheal tube settled the last point. Our neurosurgeon states that he likes our intratracheal cyclopropane better than others which we have used and others which he sees.

For our major chest surgery we have never used any anesthetic except intratracheal cyclopropane.

The use of the intratracheal tube has been one of our mainstays in the care of our patients during the anesthesia period in long surgical procedures. In brain surgery we consider it essential. It makes it possible to control the anesthesia, control respiration, and keep out of the way of the surgeon, no matter what may be the operative position. In looking at the figures, we are amazed that there were 10 cases in which the tube was not used. Most of them involved small children under special circumstances. In most other neurosurgical cases the tube is not quite so essential but makes for much greater efficiency because of prone, semiprone, or other odd position.

In open chest surgery we use the intratracheal tube consistently in spite of only 78 per cent shown in Table IV. Of the 7 patients who did not have it, some were tiny babies with tracheo-esophageal fistulas and some had extensive chest wall surgery.

All of our abdominal surgical patients come to the operating room with Wangensteen suction tubes through the nose into the stomach, and suction with the Wangensteen bottles is continued throughout the surgery. It is almost impossible to keep a perfectly fitting mask with the tube coming out under it. In addition to that, in spite of the constant suction, there is sometimes some gastric fluid which, because of manipulation, follows up the esophagus outside the tube and tends to enter the trachea unless the latter is occupied by the tracheal tube. Therefore, we use a tracheal tube in practically all gastrectomies and in the great majority of other gastrointestinal cases.

We use an intratracheal tube surrounded by an inflated cuff. The inflation is done with air under 14 to 16 cm. of water pressure. Measuring the inflation pressure was suggested by Dennis after we had injured a trachea by too great inflation with a syringe. Our tracheal tubes, cuffs, and water manometers are homemade in our division of anesthesiology. The type of cuff was worked out for our special needs by Grimm, with one of us (R. T. K.). This

provides an airtight fit without injury to the trachea, preventing the entrance of any foreign material and providing perfect control of respiration.

We have permitted the use of the cautery and the fulgurating current for all of our brain and neurologic surgery and for our gastrointestinal surgery except in a few individual instances in which we felt there might be some explosive gas present in immediate proximity to the spark or heat. We have felt that the type of anesthesia used and the benefit of the cautery or fulguration were both too advantageous to be given up, in view of the closed system of anesthesia and careful draping. With hundreds of trials we have failed to pick up an explosive sample of gas farther than three inches from the wide-open end of the gas tubing with three and four times the gas flow used in anesthesia, even though an explosive mixture was picked up each time from the tube itself. We do not believe that any inadvertent tiny leak can reach the cautery or spark.

Among the 1,000 patients with long surgical operations, 84 have had postoperative pulmonary complications, 17 of whom died and 67 recovered. The diagnoses were as follows, some having more than one diagnosis: atelectasis 27, pulmonary edema 7, bronchial pneumonia 30, pneumonia 10, pneumonitis 4, pulmonary emboli 6, and miscellaneous 6. There were 92 deaths from nonpulmonary complications.

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INTERCOSTAL NERVE BLOCK

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THE development of anesthesiology in recent years has been rapid, new agents and methods making possible operative procedures which in former years entailed either great danger or certain death. One of the most important of these has been the use of regional anesthetic procedures, which were popularized in large measure by the teachings and writings of Gaston Labat.

The field has been enlarged still further to include the use of regional procedures not only for operative interventions but also in diagnosis and therapeusis. Sympathetic block with procaine is used as a preoperative test to determine the efficacy of sympathectomy in essential hypertension. Lumbar paravertebral block relaxes the spasm associated with thrombophlebitis and helps relieve the pain from the impaired circulation. Subdural injections of absolute alcohol often eliminate the intractable pain of inoperable carcinoma.

The blocking of the intercostal nerves is one of the regional anesthetic procedures which has been developed largely in the last few years since Bartlett's[1] description in 1940. Its use in the relief of pain can be applied to a

Received for publication, March 2, 1945.

variety of conditions. It has been tried and found of value as an anesthetic for operative procedures, in the relief of postoperative pain, in the relief of acute pleuritic pain, and in the relief of the pain associated with fractured ribs. These will be discussed individually.

TECHNIQUE

A description of the anatomy of the intercostal nerves will give a better insight into the benefits to be gained from their anesthesia. After arising from the spinal cord they pass out of the intervertebral foramina and run in a groove behind and at the lower border of their respective ribs between the internal and external intercostal muscles, giving off branches to the pleura. Upon reaching the costal arch they pass below the costal cartilage into the anterior abdominal wall and run toward the midline in an oblique downward direction to innervate the skin and muscles of the entire anterior abdominal wall with the exception of the inguinal regions. The nerves are most accessible in the region from the mid-scapular to the anterior axillary lines where they run in a closed compartment under and behind the rib, and it is in this region that the blocks are done.

The proper placement of the patient is quite important, and either of two positions may be used. When the block is being done before or immediately after an operative procedure, the patient is usually in the recumbent position. If it is being done therapeutically, the patient can either sit or assume the recumbent position. The arm should be raised above the head for two reasons, first, to remove it from the operative field, and second, to make the skin over the ribs taut to facilitate both the finding of the landmarks and the insertion of the needle.

With the patient in the recumbent position, a small pillow is placed under one side to raise the thoracic cage and make the operative field more accessible. The area is draped and surgically prepared with alcohol, ether, and a suitable antiseptic solution, using strict aseptic technique. Then, using a hypodermic needle, wheals are raised with 0.5 per cent procaine over the selected ribs at the desired site of injection, usually the midaxillary line. The intercostal block is performed by inserting a needle perpendicular to the skin until it strikes against the rib. Once contact is made with the rib the needle is moved down until it just slides past the undersurface of the rib where it now lies in close proximity to the intercostal nerve. The solution is deposited here, and after the needle is withdrawn the area is vigorously massaged. The needle used is an ordinary No. 20 gauge intravenous needle with a short bevel. The anesthetic solution is varied depending upon the desired result.

There are several precautions to be observed in the technique. Aspiration should always be done before injecting to avoid intravenous administration of the drug or injection into the pleural space. Strict asepsis should be used to avoid infection. Too much of the agent should not be used and the upper limits of safety in quantities of local anesthetics should be remembered.

USE IN OPERATIVE PROCEDURES

There are many relatively poor-risk patients who need upper abdominal operations. Many of these fall into the hypertensive arteriosclerotic older age group in whom high spinal or deep inhalation anesthesia would constitute a definite hazard. In these instances local anesthesia is often used, but un-

fortunately local infiltration of the area does not always produce enough relaxation for satisfactory surgery. In this group of cases intercostal nerve block is of great usefulness. When properly done it provides relaxation of the upper abdominal musculature with sensory anesthesia which is sufficient for opening the abdominal cavity. Although it can be used alone, it is best when in some form of balanced anesthesia.

Balanced anesthesia is a term originally used by Lundy[2] to describe the use of a combination of anesthetic agents and methods so balanced that the burden of pain relief and the production of conditions compatible with surgery are not borne by any one method but rather by the combined effects of several. Intercostal block is ideally suited to this type of procedure.

The first step in the production of any balanced anesthetic is the proper preoperative preparation of the patient. The effect to be desired from the premedication is the production of a sleepy, drowsy patient who can be easily aroused. This can usually be accomplished by the combination of a barbiturate, opiate, and one of the belladonna derivatives. The dosage is determined only after a careful estimation of the patient's strength and condition. In the average case, nembutal gr. 1½, morphine sulfate gr. 1/6, and scopolamine hydrobromide gr. 1/150 have proved quite satisfactory when given from one to one and one-half hours preoperatively. The barbiturate also helps ward off any toxic effects from the anesthetic solution.

After the patient has arrived in the operating room, the block is performed in the recumbent position as already described. Usually nerves VI through XI are injected bilaterally in the midaxillary line. When proficiency in the technique has been acquired, the whole procedure does not take more than ten minutes. After the block has been done, the surgeon must wait from five to ten minutes before complete anesthesia is present as shown by relaxation of the musculature and loss of sensation to skin stimuli. The agent used has been a 2 per cent solution of procaine without adrenalin. Three cubic centimeters injected into each interspace have invariably provided more than two hours of good anesthesia.

Although in some instances if the surgeon is very careful and gentle the operative procedure may be carried out with no further anesthesia, it is best to put the patient lightly to sleep with nitrous oxide or cyclopropane. The anesthesia need only be to the first plane of the third stage of anesthesia (after Guedel[3]). Relaxation has already been obtained through the nerve block.

Evans[4] has recently published a report on the use of intercostal block plus sodium pentothal intravenously in surgery of the upper abdomen, referring especially to war injuries, where he finds the combination to be better than any other method available. In our civilian hospitals a beautifully balanced anesthesia can be produced using this combination plus a 50 per cent nitrous oxide-oxygen mixture. This case has previously been reported in a paper on intercostal block in balanced anesthesia.[5]

CASE 1.—E. G., a 64-year-old, obese, white woman with hypertensive arteriosclerotic heart disease and pyloric obstruction from carcinoma of the stomach was to have a gastroenterostomy.

Premedication was a combination of nembutal, morphine, and scopolamine. Intercostal block in this instance was done with the formula to be given later in this paper, containing monocaine base, benzyl alcohol, benzocaine and oil, 1½ c.c. at each interspace. After the skin

incision was made, she was put to sleep with a 2½ per cent solution of sodium pentothal injected into the tubing of an infusion which the patient was receiving. Immediately thereafter the mask of an anesthetic machine was applied to the patient's face and a 50 per cent mixture of nitrous oxide and oxygen was administered. This last made it possible to give her a high concentration of oxygen while providing a means of watching the depth of respiration. The nitrous oxide also lessened the amount of pentothal needed to keep the patient asleep.

The patient did very well during the operation with practically no change in the pulse or blood pressure. That evening, when she became thirsty, she got out of bed to get a drink of water. After being returned to her bed, she remained there during an otherwise uneventful recovery.

In this case the use of the intercostal block to produce relaxation allowed the use of small, relatively innocuous amounts of other agents to produce a satisfactory anesthesia. The use of any one agent to produce the same effect could not have been done without having an undesirable effect upon the patient.

The intercostal block can be used with any type of inhalation anesthesia and has proved very helpful with nitrous oxide, cyclopropane, and ether.[5] The demand for great depth of anesthesia to produce upper abdominal relaxation is removed, and the beneficial effects to the patient are evident both in the condition during the operation and in the postoperative period.

USE FOR POSTOPERATIVE PAIN

After using the intercostal block in operative procedures for some time, the thought arose that if a long-acting anesthetic were used to produce anesthesia or analgesia of several days' duration, the patient could be spared the ordeal of postoperative pain, and with the relief of this pain would come freedom from its sequelae. The pain following upper abdominal operations and attempts to relieve it result in greatly reduced respiratory excursions. The factors involved are splinting of the diaphragm, tight abdominal dressings and binders, reluctance to take deep breaths, morphine, and other opiates, unwillingness to attempt to cough up gathering mucus, and the tendency of the patient to remain in one position. All of this leads to stasis of pulmonary secretions, atelectasis, and pneumonia. It was thought that if a prolonged anesthesia or analgesia of the operative area could be produced and these dangers eliminated, the incidence of postoperative pulmonary complications could be reduced while the postoperative period was made much more tolerable for the patient.

A survey of the literature revealed that Zollinger,[6] in 1941, had apparently had a similar idea and attempted to produce anesthesia with a solution of eucupine in oil. Although his results were not uniformly good, he felt that the principle was sound and that the method warranted further investigation and clinical trial.

Accordingly, a search was made for a suitable agent, and a preparation with the following formula* finally selected:

Monocaine base	0.02 Gm.
Benzyl alcohol	0.05 Gm.
Benzocaine	0.03 Gm.
Oil of sweet almonds	to 1.0 c.c.

This solution had previously been used by Brenner[7] in rectal work, and it was thought that it would prove satisfactory here.

*This formula is prepared and marketed under a trade name by the Novocol Chemical Mfg. Company, Inc., Brooklyn, N. Y., and a supply was generously provided for our use in these investigations.

Although there is some danger of abscess formation and sloughing when using oily solutions if too large a quanity is pooled in one place, it was felt that if only small quantities were injected in one place under aseptic conditions and then the area were thoroughly massaged, this danger could be eliminated. This proved to be true, for up to the present time more than 500 injections of this solution have been made with no local or systemic reactions of any kind being noted.

The injections were made according to the described technique, nerves VI through XI being injected bilaterally in the midaxillary line with 1½ c.c. deposited at each space. The injections were usually made after the anesthetic being used for the operation had been induced, so that the patient would be spared the pain associated with the insertion of the needles. In the case of spinal anesthesia it was done after anesthesia was present to the level of the fourth thoracic segment, and when an inhalation method was being used it was done after the patient was asleep. In a few instances it was done at the close of the operation before the patient reacted.

A marked success was obtained in a series of twenty cases, a report of which has been published elsewhere.[8] The patients were grateful for the comfortable postoperative period, and in those cases where the block was successful the incidence of pneumonia was zero. The method is still being used with the same good results.

As near as could be determined, the anesthesia produced lasted from eight to twelve hours, and was followed by a period of analgesia lasting for two to three days. These patients required little or no opiates for sedation.

This method of attempting to relieve the postoperative pain from upper abdominal operations seems to be the most practical and the most likely to succeed that has been advocated thus far. However, a much wider clinical trial is necessary before it can be properly evaluated.

USE IN FRACTURED RIBS

The same line of reasoning that prompted the use of a long-acting anesthetic for upper abdominal operations led to its use for fractured ribs. Even after adequate strapping of the chest many patients complain of pain at rest, or more often on motion, deep breathing and coughing. An attempt was made to alleviate this pain by intercostal block with the anesthetic oil solution, using the knowledge gained in its previous use. A limited number of patients have been treated in this fashion, with uniformly good results. The blocks were done with the patient in the sitting position, and 2 c.c. of the anesthetic oil solution were injected into each interspace. A typical case report is Case 2.

CASE 2.—J. S., a 59-year-old white man, came to the accident room complaining of pain in the left side of his chest since trauma three days previously. The patient had been strapped with no relief and had had no sleep since the accident. X-ray examination showed that ribs 7 and 8 on the left side had been fractured in the midaxillary line.

Intercostal block of nerves VI, VII, VIII, and IX was performed in the posterior axillary line with 2 c.c. of the anesthetic oil solution at each space, with the patient in the sitting position holding his arm above his head. In ten minutes he felt much better, and in twenty minutes the pain was gone. After restrapping he left the hospital free from pain, and smiling. He telephoned several days later to state that he had remained completely free from pain and was very comfortable.

In this type of case the intercostal block can be used to advantage if the fracture is anterior to the posterior axillary line and the injection can be per-

formed posterior to it. It must be remembered that there is an overlapping of the distribution of the intercostal nerves and that the block should always include one nerve above and one nerve below the ribs involved. It is a useful addition to the treatment of this condition and in the relief of the pain accompanying it. The treatment of the fracture itself is not changed in any way, and immobility by strapping or some other means is still to be desired.

USE FOR ACUTE PLEURITIC PAIN

One of the cardinal symptoms of a pneumonic process in the lungs is pleuritic pain, which often is quite severe and distressing to the patient. Price[9] has reported a series of cases in which he used intercostal block in an attempt to relieve this pain with marked success. The method is simple and effective, often producing permanent relief. By allowing relatively free motion of the thoracic wall, which would otherwise tend to be splinted as a result of the pain, it favors adequate ventilation and aeration of the lungs, affording protection against the complication of atelectasis. Drainage of the involved area is promoted since coughing is rendered nearly painless. Opiates which ordinarily are given for pain depress the cough reflex and thus favor stasis with resulting atelectasis.

The nerves to be injected are those corresponding to the intercostal spaces over which definite tenderness can be elicited by slight pressure. The injection is made most conveniently in the posterior or midaxillary line. However, in cases where the hyperesthesia is located more posteriorly, injection can be made in the mid-scapular line. The injections are made with 2 c.c. of a 1 per cent solution of procaine hydrochloride, with the patient in either a sitting or a recumbent position.

Although my experience has not been as favorable as that of Price, since in most cases only partial relief from pain was obtained, the method has definite value if the patient can be helped even in small measure.

CONCLUSION

The recognition of the value of intercostal block as a regional anesthetic procedure has been slow in coming. Some have been hesitant to make use of it because of the danger of striking blood vessels or puncturing the pleura, others because of the extra time and trouble involved in its performance. If ordinary precautions are taken, the method is without any more hazard than any other procedure involving the injection of an anesthetic solution into the body. The time and trouble element should not be of major importance when the benefits to be derived are so great.

The discussion here has included the use of intercostal block as an anesthetic for operative procedures, for the relief of postoperative pain, and for the relief of pain from pleurisy and fractured ribs. It is hoped that this form of therapy will find wider favor and a larger field of application. Its simplicity and ease of accomplishment should make it a common procedure in the field of anesthesiology.

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NOTES REGARDING THE USE OF INTRAVENOUS SODIUM PENTOTHAL ANESTHESIA IN MAJOR SURGICAL CASES

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WE STARTED to use intravenous sodium pentothal as a general anesthetic for major surgical cases June 5, 1942, at the Missouri Baptist Hospital. It has been used in all surgical cases by myself, and several other surgeons have used it extensively for a grand total of 2,287 cases. It has been used in every type of major surgical case, excluding lung resection. The ages of the patients ranged from 7 to 92 years. It has been used in head and neck cases, goiters, breast resection, and all types of major abdominal operations including common duct stones with jaundice and some with high nonprotein nitrogens, shock and low hemoglobin cases, which were suitable for any other general anesthetic agent. There have been no deaths traceable to this anesthetic, no thrombosis, nor local necroses. We have used morphine and atropine but we usually give hyoscine and morphine in suitable doses according to the age of the patient and his general condition about thirty to forty minutes before operation, and a sleeping dose of some barbiturate the night before operation.

In the beginning, we used a 5 per cent solution, which was soon changed to a 2½ per cent solution due to prolonged sleeping periods after operation. The dosage has ranged from 2½ to 45 gr. in one case. Anesthesia has been maintained up to four hours without ill effect. We are now averaging from 15 to 25 gr. in most major cases, such as gall bladders, hysterectomies, etc. Anesthetists must be properly trained, alert, and capable. Relaxation is very satisfactory. There is practically no postoperative nausea. The agent is nonexplosive and the equipment required is simple and inexpensive. We use the Thomas apparatus. The anesthetist is well away from the field of operation. In our early cases, from 10 to 15 gr. more of the drug were used than we now find necessary. The postoperative sleeping period ranges from one-half to four hours depending upon the preanesthetic dosage, the type of patient, and the type of operation.

The skin surface is carefully sponged with alcohol and usually the median vein is selected for puncture. When blood appears in the syringe, from 2 to 3 c.c. of sterile, chemically pure, distilled water is injected followed by the 2½ per cent pentothal solution made with sterile, chemically pure, distilled

Received for publication, Oct. 7, 1944.

water in ampules. Complete anesthesia with good relaxation is obtained in from ten to thirty seconds and usually after having used from 2½ to 7½ gr. of pentothal in 2½ per cent solution. Alcoholics and some other types require heavier initial dosage. Appropriate amounts of solution are then injected from time to time to maintain suitable relaxation, usually 2 to 3 c.c. at a time. In all major cases, 100 per cent oxygen is given throughout, due to shallow respiration caused by sodium pentothal. When the operation is almost completed, after peritoneal closure, the lungs are ventilated with oxygen, 95 per cent and carbon dioxide, 5 per cent. Any indication of overdosage is met by giving 100 per cent oxygen under moderate pressure and an open airway. The airway is used throughout the operation and the patient is sent to bed with the airway in position unless earlier ejected by him. Oxygen and carbon dioxide are administered routinely at intervals for about twenty-four hours postoperatively in all upper abdominal cases.

Much time is saved and there is no unpleasant sensation for the patient after the initial puncture. The patients seem uniformly well pleased and in fact many new patients are now requesting this drug. In prolonged procedures such as stomach resections, etc., after the initial induction with 2½ per cent solution, a continuous flow of ½ per cent solution is sometimes used, by Murphy drip, the rapidity of flow being regulated from time to time by the anesthetist.

We have four nurse-trained anesthetists who quickly grasped the technique of promptly puncturing the veins under aseptic precautions, first injecting 2 or 3 c.c. of sterile water to make certain that the needle is properly in the vein before the pentothal solution is used. They soon learned to judge when to give additional amounts in order to maintain relaxation with a minimum amount of the drug. Increased respiration and increased muscular tension are indications for additional dosage.

It is our considered judgment that sodium pentothal can be used safely in major surgery and to greater advantage than any other anesthetic agent now available. Careful records have been made and are available in all cases.

CURARE IN ANESTHESIA

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THE employment of curare* as an anesthetic accessory for the enhancement of muscular relaxation is now becoming more universal. The technique appears to be withstanding the rigors of use in increasing numbers of cases in favorable and unfavorable circumstances by both the experienced and inexperienced anesthetist. The exact allocation of the drug's importance in the field of anesthesiology cannot yet be determined, but clinical and laboratory experience with the drug has uncovered certain desirable and undesirable properties, knowledge of which will assist in establishing its safe and rational utilization. It is the purpose of this communication to outline these properties.

Sustentative evidence[1-4] gives credence to the theory that the basic action of curare is its ability to minimize or prevent response to acetylcholine. Curare is apparently capable, then, of influencing any structure whose function depends on mediation of nerve impulses by acetylcholine. This concept is helpful in comprehending the effect of the agent on organs ennervated by the somatic or the autonomic nervous systems. The effect of the drug is directly proportional to the concentration of the drug at the site of action. The action is reversible and can be accomplished by increasing the concentration of, or the length of action of, acetylcholine. This increase in concentration or prolongation of action of acetylcholine can be produced by strengthening the nerve impulse, adding acetylcholine artificially, or inhibiting the action of cholinesterase with drugs such as physostigmine or prostigmine. This latter method is the most convenient means of overcoming excessive curarization in clinical practice. There is some evidence that curare may kill by depressing the peripheral circulation,[5-7] but the majority of deaths from curare are due to asphyxia accompanying unrelieved respiratory paralysis.[8]

The coveted action of curare in clinical practice is that degree of depression of muscular activity that provides suitable relaxation at the site of operation without undue paralysis of the muscles of respiration or prostration of the peripheral circulation. Fortunately, this optimal state can be achieved by judicious use of the drug, and the frequency of its attainment is directly proportional to the experience of the employer. The technique by which this state can be obtained has been amply covered in other publications and remains a standard procedure.[9-14] Muscular paralysis is achieved by preventing the receptor substance of the muscle from responding to acetylcholine. The muscle cells are unaffected and may be stimulated to full action, in the presence of curarization, by electrical means. The nerve leading to the muscle is likewise unaffected by the curare. It is of considerable interest and importance in the clinical use of curare to know that certain of the anesthetic agents, notably ether, possess curariform actions of their own and the amount of curare used in conjunction with these agents must be significantly reduced.[4]

Experimental and clinical data[5, 15, 16] seem to indicate that curare has no direct or indirect effect on the heart. The drug has been used on patients

Received for publication, Nov. 9, 1944.

*Intocostrin, E. R Squibb & Sons, New Brunswick, N. J.

with and without cardiac abnormalities and in the presence of agents that are prone to produce arrhythmias, and no alterations attributable to the curare can be segregated. Peripheral circulatory depression, however, does develop in a few patients in whom curarization is present. This reduction in blood pressure may be due to a direct relaxing effect on the smooth muscle of the arterioles or to widespread muscle relaxation with consequent impaired venous return and lowered cardiac output. It is associated with either excessive single doses administered in a short time or to rather complete curarization over long periods of time such as is necessary in the treatment of tetanus with this drug. The circulatory detrusion is usually of brief duration and recovery occurs without specific therapy. In patients with labile vascular systems, it may be profound and refractory to treatment. In the latter type of case, it might be possible to precipitate a fatal termination of the anesthetic procedure. It is important, for this reason, to use the curare cautiously and avoid large single doses or protracted curarization.

The action of curare on the gut has been studied.[6] The small intestine consistently exhibits brief cessation of peristalsis and somewhat longer periods of loss of tone with therapeutic amounts of the drug in the unanesthetized animal. The cessation of peristalsis lasted usually only two to three minutes. In a few animals it lasted approximately twenty minutes. The loss of tone persisted for about twenty minutes with a gradual return to normal. Morphine and cyclopropane obliterated the curare effect. The effect of curare on the stomach was inconclusive. The etiology of the cessation of peristalsis and the loss of tone produced by the curare may be one or the other or a combination of two factors. The drug was shown to have a direct effect on isolated small bowel and it is known also that curare inhibits to some extent the action of the vagus nerve.[2, 6] It is impossible with the available data to determine which of the factors is dominant. It is anticipated that no residual action of curare will remain which might predispose toward postoperative ileus.

There is minimal detoxication of curare in the liver and most of it is excreted unchanged by the kidney. Although it might be surmised, there is no evidence as yet that liver or kidney damage results in cumulative depression.

The effect of the drug on the uterus has not been studied. A number of patients have been given curare for purposes of abdominal muscle relaxation during cesarean section without any apparent effect on the infant.[17] Studies have not been made on alterations of the blood elements and chemistry by curare.

Curare has no analgesic property and in situations in which pain relief is necessary, the relief must be secured by the most appropriate agent and technique. Curare may be used with any of the inhalation agents, with pentothal sodium, with intrathecal techniques if analgesia is present, tribromethanol in amylene hydrate, and with topical, regional, or infiltration techniques. As pointed out earlier, the dose must be adjusted according to the curariform properties of the agent used. The action of curare is restricted to approximately twenty minutes. It is advisable then, when using inhalation anesthesia, to use an agent that has the ability to provide moderate muscular relaxation by itself. The curare is preferably used to produce only added relaxation when the occasion demands. When the less potent inhalation agents are used, all the relaxation must be obtained with the curare, and the hazards attending its excessive and prolonged use appear. The use of curare with a topical anes-

thetic technique is limited chiefly to endoscopic manipulations during which it is difficult to obtain sufficient relaxation to permit easy and nontraumatic examination.[18]

SUMMARY

Curare has proved useful as a means of obtaining improved muscle relaxation during anesthesia. It is a safe drug when used in the proper fashion. Its chief disadvantage is the relatively narrow margin between the optimal dose and the dose producing respiratory paralysis. It should be used only when means of producing efficient artificial respiration and prostigmine are immediately at hand. It should be used only by those experienced in the science and art of inhalation anesthesia and should not be used to cover up errors of commission and omission in the anesthetic technique. It will gain and retain respect as a useful adjunct to anesthesia if it is employed within the limits of its pharmacologic properties and is not abused by excessive and indiscriminate use.

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ANESTHETIC AGENTS AS FACTORS IN CIRCULATORY REACTIONS INDUCED BY HEMORRHAGE

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INTRODUCTION

EXPERIMENTS designed to investigate shock in the laboratory have regularly utilized anesthesia as a means of immobilizing the animal for the technical procedure. Although an extensive variety of drugs has been employed for this purpose, minor consideration has been given to the fact that the influence of anesthesia on different functions of the organism varies widely with the agent employed.

Recent reports by Wiggers,[1] Blalock,[2] and Allen[3] have directed attention to the necessity for standardizing the anesthetic technique so as to obtain a uniform degree and duration of narcosis. These and other reports, however, have neglected the specific complications which arise from anesthesia during the experiment. Without more objective knowledge of the variables introduced, it is difficult to evaluate and compare the conclusions and concepts proposed by different investigators.

Despite the renewed interest in the importance of anesthesia with respect to the circulation, no detailed study has appeared on the specific effects of anesthetic agents on the peripheral circulation, either in normal animals or those in shock. Recently, Bennett, Bassett, and Beecher[4] determined the effects of several anesthetic drugs on the changes in blood flow in several major blood vessels of dogs following hemorrhage. The present study was undertaken to clarify the effects of some commonly used anesthetic agents on the circulation by utilizing changes in the circulatory dynamics of the capillary bed.

METHODS

The changes in the peripheral circulation resulting from a standardized bleeding procedure were followed in seventy dogs anesthetized with six different drugs. Plasma protein and hematocrit readings were routinely obtained prior to bleeding and induction of anesthesia. Plasma protein was determined by the falling-drop method of Barbour and Hamilton, and the hematocrit value by centrifuging in Sanforth-Magath tubes. The femoral artery was cannulated after local tissue infiltration with 2 c.c. of a 1 per cent solution of procaine, and blood pressure was recorded continuously, using heparin as an anticoagulant in the cannula. Following the induction of anesthesia, the omentum was exteriorized for direct microscopic study according to a method previously described.[5] The essential feature of this method is the withdrawal of part of

This work was aided in part by a grant from the Josiah Macy, Jr. Foundation, New York. A preliminary report appeared in Proc. Soc. Exper. Biol. & Med. **56**: 73-77. 1944. It constitutes the seventh of a series of studies on various phases of experimentally induced shock. The first study is listed as Ref. 5, the fourth as Ref. 11, the fifth as Ref. 12, and the sixth as Ref. 13 in the reference list of the present paper. The second study on acute hemorrhage, appeared in Am. J. Physiol. **139**: 123-128, 1943; and the third on blood pressure technique, in J. Lab. & Clin. Med. **28**: 886-888, 1943.

Received for publication, July 12, 1944.

the omentum into a rubber sheath attached to the peritoneal margins of the abdominal incision and exposure of a small portion of omental tissue over a glass horseshoe resting in a specially prepared moist chamber. The exteriorized omentum is maintained at body temperature and the exposed region kept in a moist condition by a continuous drip of warm Ringer's solution buffered with sodium bicarbonate to a pH of 7.3 and containing sufficient gelatin (1 per cent) to give it a colloidal osmotic pressure similar to that of a serous exudate. With these precautions, it is possible to keep the capillary circulation under observation for five or six hours with its normal reactivity intact. The omental criteria studied were (a) the rate and distribution of blood flow, (b) vasomotion, and (c) epinephrine reactivity of the muscular components of the capillary bed.

Dogs receiving only local anesthesia served as a control series with which the anesthetized groups could be compared. The controls were prepared for observation of the omentum with an abdominal field block using 8 to 10 c.c. of 1 per cent procaine solution and received no further medication.

As an additional means of observing the effects of hemorrhage on unanesthetized dogs, the omentum was prepared for observation in eleven animals by administration of cyclopropane or pentothal only during the required surgery. The dogs so prepared during cyclopropane anesthesia were allowed to recover consciousness for one hour before the bleeding was begun. Their behavior was very similar to that of the dogs receiving local anesthesia only, and the data concerning them were not included. Pentothal was found to be unsuitable for such preparations since its effects on the peripheral circulation persist for several hours after the dog has recovered consciousness.

The experimental dogs were divided into five groups, each of which was subjected to a different anesthetic procedure. The drugs used were: morphine sulfate (ten dogs), cyclopropane (nine dogs), ether (five dogs), sodium pentobarbital (twelve dogs), and sodium pentothal (eight dogs). Anesthesia was continuous throughout the experiment.

Morphine sulfate, 2 mg. per kilogram of body weight, was injected intravenously. This dose produced mild depression in the animal and a euphoric state which could not be considered complete anesthesia.

Cyclopropane and ether were administered, intermittently with oxygen, by means of a standard Foregger metric anesthesia table with a closed to-and-fro rebreathing system and a cannister for carbon dioxide absorption. Following the induction of anesthesia with a special face mask, an endothracheal catheter was introduced to assure an adequate airway throughout the experiment. The uppermost (first) plane[6] of surgical anesthesia was maintained, in which spontaneous respiration is not depressed and the blink and corneal reflexes are brisk. The oxygen content of the respired anesthetic mixtures was always far in excess of metabolic requirements (75 to 90 per cent).

Sodium pentobarbital was given in a single intravenous dose of 25 to 30 mg. per kilogram of body weight. This amount produced about forty minutes of fairly deep surgical anesthesia, which gradually diminished over the succeeding two and one-half to three hours. As the surgical procedure and initial observations normally required forty to fifty minutes, these animals at the time that bleeding was instituted were in a depth of anesthesia comparable to that of the other anesthetized dogs. Five of the dogs in this group, to whom oxygen was given by endotracheal catheter, exhibited no demonstrable differences from those breathing air.

Sodium pentothal (1 per cent solution) was administered intermittently by vein from an infusion drip bottle in volumes sufficient to maintain a degree of narcosis similar to that induced by the inhalation agents. This required an average of 9.6 mg. per kilogram per hour, a relatively small dose of pentothal. All of these dogs received oxygen.

The bleeding procedure consisted of an initial blood loss of 2 per cent of body weight and the subsequent removal of 0.5 per cent at thirty-minute intervals. Bleedings were continued until a cessation of blood flow occurred in the large omental arteries. This was considered the maximal blood loss, since experience in bleeding over 150 dogs has demonstrated that further hemorrhage invariably results in a precipitous collapse of the animal. No sustaining infusions were given, and the dogs were left until they either showed signs of circulatory collapse or had maintained an adequate blood flow for at least two hours after the final blood loss. The dogs which collapsed spontaneously were infused with the blood withdrawn. The remainder of the dogs were given a similar infusion three hours after the last bleeding. Note was made of the degree of improvement of the peripheral circulation and of blood pressure for forty-five to ninety minutes. Autopsies were done on representative dogs in each group.

In addition to noting blood loss, blood pressure, and the omental criteria, atrial blood samples were taken every twenty-five to thirty minutes after each bleeding through a catheter passed down the right jugular vein to the level of the right atrium. These samples were analyzed for (a) venous oxygen, (b) uric acid, and (c) vasoexcitors and vasodepressors. The oxygen determinations were made by Roughton and Scholander's syringe method.[7] Plasma uric acid levels were determined with an electrophotometer, using the colorimetric method of Brown. The sensitive reactions of the peripheral blood vessels to abnormal substances in the blood were utilized for detecting the presence of vasoexcitors and vasodepressors. Serum obtained from the hemorrhaged dogs was injected into normal rats and the effect on the rat mesoappendix noted.[8]

RESULTS

Table I presents data on fifty-seven normal dogs divided into a control series (thirteen dogs) and an experimental series (forty-four dogs). It was found convenient to classify the data into separate categories, each corresponding to a single circulatory criterion. Within each category, the results were tabulated as average figures. A sufficient number of cases to obtain uniform results was included in each anesthetic group. The hematocrit and plasma protein values were within normal limits. It will be noted that initial venous oxygen values were fairly high in those animals receiving oxygen endotracheally, an observation previously described.[9]

Tolerance to Blood Loss.—The maximal blood loss for each animal was determined. By bleeding the dogs at thirty-minute intervals, it was possible to withdraw from 3.2 to 6.7 per cent of their body weight in blood without causing the abrupt death of the subject. These values should not be confused with the bleeding volume which other investigators have obtained by exsanguination. With the method used in this study, all of the dogs survived for one or more hours after the last bleeding.

As noted in Table II, the ability of the animal to withstand hemorrhage varied significantly according to the anesthetic agent employed. The largest maximal blood loss was obtained in the control group. The animals in this group also showed the longest survival period and readily recovered following

TABLE I. AVERAGE NORMAL VALUES PRIOR TO HEMORRHAGE

ANESTHESIA	NO. OF DOGS	NORMAL MEAN BLOOD PRESSURE (MM. Hg)	NORMAL HEMATOCRIT (%)	NORMAL PLASMA PROTEIN (GM. %)	ANESTHETIC DOSE	OXYGEN	NORMAL BLOOD URIC ACID (MG. %)	NORMAL VENOUS OXYGEN (VOL. %)
Controls:								
Procaine abdominal block	13	147	50 ± 3	6.00 ± 0.5	8-10 c.c. 1% procaine	Not used	1.2	13.99
Experimentals:	44							
Morphine	10	142	45 ± 3	5.80 ± 0.5	2 mg. per kg.	Not used	0.8	14.4
Cyclopropane	9	152	43 ± 6	5.55 ± 0.5	Plane I, stage III, surgical anesthesia	Used	0.9	17.18
Ether	5	139	49 ± 2	5.67 ± 0.3	Plane I, stage III, surgical anesthesia	Used	0.85	19.20
Pentobarbital	12	147	44 ± 1	5.80 ± 0.4	25-30 mg. per kg.	Used 5 dogs	1.2	16.15
Pentothal	8	164	48 ± 3	5.76 ± 0.4	9.6 mg. per kg. per hr.	Used	1.0	15.3

TABLE II. DATA FOLLOWING HEMORRHAGE

ANESTHESIA	MAXIMAL BLOOD LOSS	% SPONTANEOUS COLLAPSE < 3 HR. AFTER LAST BLEEDING	% REVERSIBLE TO TRANSFUSION 3 HR. AFTER LAST BLEEDING	CRITICAL BLOOD PRESSURE LEVEL (MM. Hg)
Procaine abdominal block	5.3	23	92	35-45
Morphine	4.6	60	70	40-50
Cyclopropane	4.8	33	89	40-45
Ether	4.1	80	20	75-85
Pentobarbital	3.8	75	25	55-65
Pentothal	4.0	100	0	80-85

"Maximal Blood Loss" represents average figures. "% Spontaneous Collapse, etc.," notes the frequency of circulatory collapse within three hours after final bleeding. Infusions were administered to dogs when collapse occurred and to all other dogs at the end of three hours. "% Reversible, etc.," indicates the percentage of dogs which could be recovered by transfusion. "Critical Blood Pressure Level" is that below which circulation deteriorated rapidly.

transfusion. Several of the dogs in the control group were observed for over twelve hours. These required no sustaining infusion and showed no signs of deterioration. In the morphine group, although the dose produced only a euphoric state and not complete anesthesia, it did significantly lower the dogs' ability to tolerate hemorrhage as compared with the controls. Of the four groups subjected to inhalation or intravenous anesthesia, the dogs in that group given cyclopropane showed a resistance to blood loss which most closely approximated that of the control group. These dogs survived for at least three hours and always responded well to transfusion. As indicated in Table II, 33 per cent of this group collapsed spontaneously and 89 per cent recovered as a result of transfusion alone. The ether-treated animals averaged a maximal blood loss of 4.1 per cent, and their survival time never exceeded two hours. Moreover, they were refractory to transfusion and did not respond when their original blood volume was finally restored.

The animals in the two groups subjected to barbiturate anesthesia withstood less hemorrhage than the others. Those given pentobarbital showed fairly uniform blood loss figures, averaging 3.8 per cent. Seventy-five per cent of the animals in this group collapsed spontaneously within three hours after the last bleeding, and the same proportion was irreversible to transfusion. The dogs receiving pentothal were less uniform both as to tolerance to blood loss and as to survival time. During pentothal anesthesia two patterns of behavior were noted, as previously reported,[10] although the data in Tables I and II show only average figures for the group as a whole. One pattern of behavior (five dogs) was characterized by high initial blood pressures (170 to 175 mm. Hg) after the onset of anesthesia and by greater tolerance to hemorrhage and longer survival time than was noted in the remaining members of this group. The second pattern of behavior resulting from pentothal was characterized by an initial fall in blood pressure (to 105 to 112 mm. Hg), smaller blood loss figures, and shorter survival times. Both of the barbiturate groups showed a progressively poorer response to transfusion in the interval after the last bleeding. With pentothal, all of the dogs collapsed spontaneously and none was reversible with infusion.

When ether or barbiturate anesthesia was employed, extreme care was required in estimating the maximal blood loss. This was especially true with ether, where the loss of as little as 4 to 5 c.c. of blood per kilogram in excess of the omental end point frequently resulted in the sudden collapse of the animal.

For each anesthetic procedure, a characteristic range of blood pressure levels was maintained for a variable time after maximal blood loss before collapse ensued. This is referred to in Table II as "critical blood pressure" and represents a blood pressure range below which the condition of the dog rapidly deteriorated.

Inadequacy of Blood Pressure as a Circulatory Criterion.—Blood pressure proved to be the least reliable of all the circulatory criteria employed. Following equivalent blood loss, the fall in blood pressure varied considerably from animal to animal so that no accurate correlation could be made between the blood pressure levels and blood loss during anesthesia with any one agent. Even less reliable were comparisons between blood loss and blood pressure during different anesthetic procedures (see Fig. 1). For example, with hemorrhage of 3.5 per cent (Table I), the blood pressure with abdominal field block

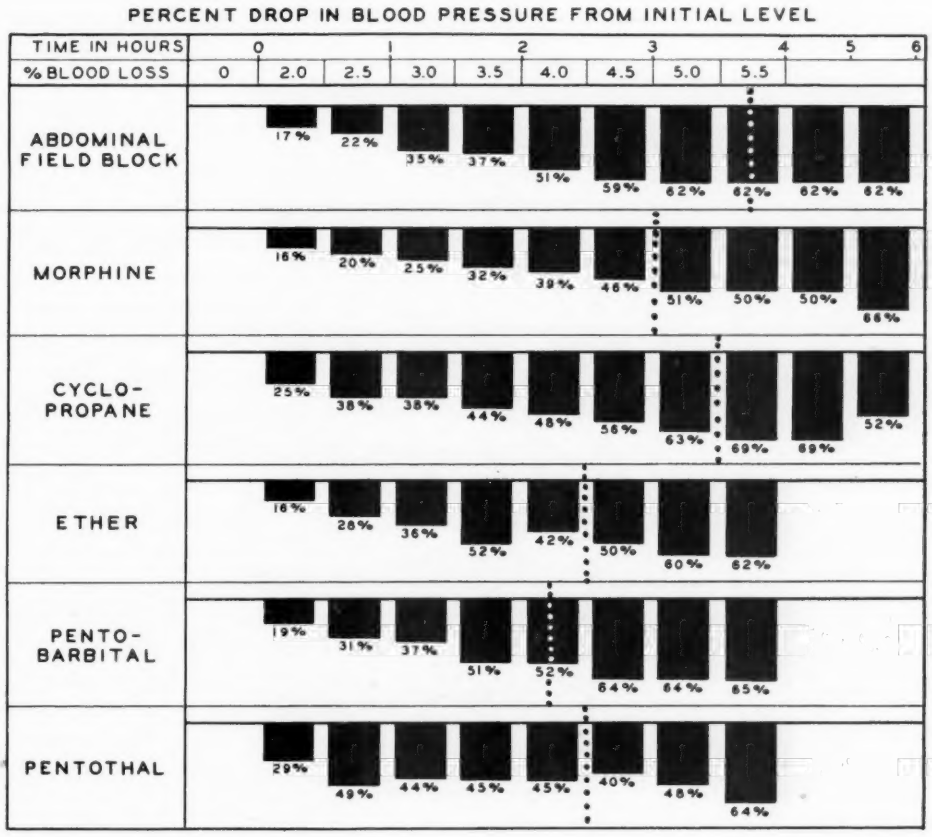

Fig. 1.—Dotted vertical lines in each group indicate final bleeding. Changes during bleeding are shown to the left of the line and those occurring after final bleeding to the right.

was 75 mm. Hg; with cyclopropane, 110 mm.; and with pentobarbital, 54 mm. Further evidence of the unreliability of blood pressure levels was obtained by comparing two dogs with similar blood pressures under the same anesthesia. After being given pentothal and bled 3.0 per cent, Dogs 126 and 138 both had blood pressures of about 85 mm. In spite of this, their other circulatory data revealed a markedly dissimilarity.

Blood pressure readings were also not a reliable index of the dogs' ability to withstand further hemorrhage and did not serve as a prognostic indication of survival time. For example, animals during ether or pentothal anesthesia usually showed blood pressures of 85 to 95 mm. following the last bleeding.

This criterion by itself indicated no immediate danger of circulatory collapse. However, not only was further bleeding contraindicated, but most of these animals died within forty to eighty minutes. In the groups receiving procaine and morphine, comparatively low blood pressure levels (35 to 50 mm.) were reached before maximal blood loss was attained. The low blood pressures alone would have condemned further hemorrhage and indicated a short survival time. Actually, these dogs tolerated additional blood loss up to 1 per cent of body weight and were among those which survived longest.

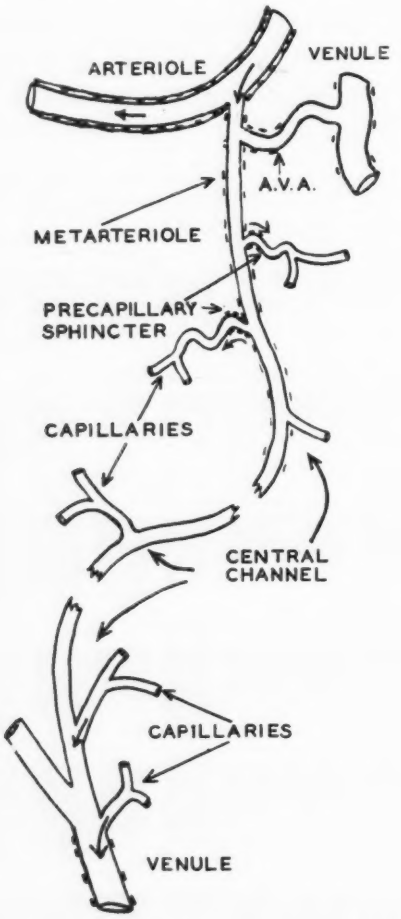

Fig. 2.—Structural pattern of a typical unit. Nomenclature and distribution of muscular components are indicated.

During each bleeding the blood pressure dropped abruptly to very low levels. When bleeding was discontinued, this condition was succeeded by an immediate increase in blood pressure. The rate and height of this rebound varied with the anesthetic agent used. The loss of this compensatory rebound in blood pressure usually occurred as the dogs approached their maximal blood loss.

Peripheral Circulatory Criteria.—Previous studies[11-13] on the circulatory changes in hemorrhagic and tourniquet-induced shock have demonstrated that the specific reactions of the different components of the capillary bed are sufficiently pronounced to serve as criteria for identifying progressive stages in the syndrome (see Fig. 2 for terminology). The degree to which the peripheral blood vessels participate in the compensatory reaction following blood loss is reflected in the adequacy of the flow through the capillary bed, that is, rate

of flow and the ability to restrict the circulation to the most direct capillary channels.

The peripheral mechanism restricting the blood flow to certain channels of the capillary bed is the maintenance of an augmented vasomotion of its muscular components. Vasomotion consists of a periodic contraction-relaxation cycle of muscular metarterioles and precapillaries. Such vasomotion, by controlling the patency of the centrally located vascular channels and their branches, conditions the distribution of blood through the entire capillary network. Loss of vasomotion results in an overfilling of the bed.

The reactivity of the smooth muscle elements of the capillary network was studied by noting their reaction to epinephrine topically applied. The minimal effective concentration of epinephrine was determined for each dog prior to bleeding by applying the drug to the surface of the omentum and noting the concentration which produced a narrowing of the metarterioles just sufficient to slow capillary flow.

Early in this study it was observed that variations in the peripheral circulation occurred simultaneously with changes in the depth of anesthesia. For this reason it was found essential to maintain the dogs consistently in the upper first plane of surgical anesthesia. Despite this, the different anesthetic agents produced characteristic differences in the normal peripheral circulation.

Variations in Unbled Dogs With Different Anesthetic Agents.—Blood flow, except in the pentothal and ether groups, was rapid and periodically became restricted. With pentothal and ether, flow was rapid but not restricted.

With ether and pentothal, vasomotion was slowed and in some instances was not present. During cyclopropane anesthesia, vasomotion was more active than in the controls, while in those dogs given morphine no difference from the controls was noted. The dose of pentobarbital caused a slight diminution of vasomotion.

The morphine and control groups showed comparable epinephrine reactivity, the minimal effective concentration being between 1 part in 3 million and 1 part in 6 million. In the pentothal and cyclopropane groups high reactivity was noted, ranging from 1 part in 10 million to 1 in 20 million. Ether and pentobarbital anesthesia lowered the reactivity (1:2 to 4 million) below that of the control group.

Omental Blood Flow as an Index of Circulatory Efficiency.—The feature which most accurately reflected the condition of the animal following hemorrhage was the ability to maintain an effective capillary blood flow. Blood loss up to 2.5 per cent had no significant effect on capillary blood flow in any experiment. The effect on the peripheral circulation was restricted to a narrowing of the large muscular arteries to about one-half their original diameter and a less marked narrowing of the accompanying veins. With more severe blood loss, slowing of the capillary flow occurred during each bleeding and was succeeded by a partial restoration of the former rate of flow. As blood loss approached maximal volumes, blood flow in the larger vessels was considerably slowed, while that in the capillary bed showed a transient stagnation. When maximal blood loss was attained, the entire peripheral flow ceased during the bleeding.

Fig. 3 depicts the progressive changes in blood flow resulting from hemorrhage during the different types of anesthesia. The least disturbance in blood flow occurred in those groups (procaine, cyclopropane, morphine) which

had the highest blood loss figures. The omentum became relatively ischemic as a result of the extreme vasoconstriction of the larger vessels. However, the capillary blood flow remained comparatively rapid by virtue of the restriction of the circulation to the most direct capillary channels. Under these conditions, the venular outflow remained adequate even at blood pressures as low as 35 to 40 mm.

Those groups which showed poor tolerance to bleeding developed an inadequate capillary circulation soon after maximal blood loss. During ether anesthesia, blood flow slowed sooner than during any other type of anesthesia. A unidirectional flow through the larger vessels persisted up to the point of maximal blood loss. The pentothal group showed an abrupt deterioration of capillary blood flow soon after reaching maximal blood loss. Capillary flow never developed the same degree of restriction as in the controls. A progressive decrement in capillary flow occurred in the pentobarbital group after the third bleeding (3 per cent).

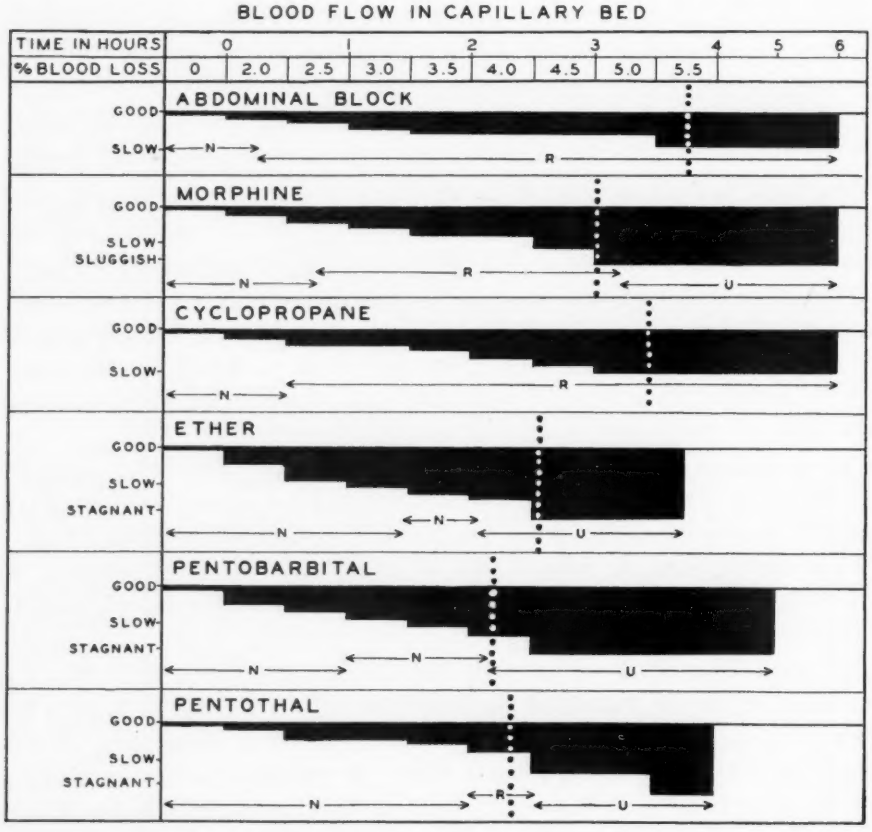

Fig. 3.—Changes in rate of blood flow are indicated by extent of deviation below normal base line. Dotted vertical lines indicate average maximal blood loss. N, normal distribution of circulation; R period of restricted capillary flow; and U, unrestricted, with a loss of ability to confine flow to central channels.

With ether, pentobarbital, and pentothal, spontaneous collapse occurred in almost all the dogs twenty to ninety minutes after the final bleeding. The incipient circulatory failure was detected in the omentum by the development of stagnation in many of the capillaries and venules and by the occurrence of backflow from the larger veins. Spontaneous collapse occurred only in a small percentage of the dogs given procaine and cyclopropane. In instances where is occurred, the collapse was sudden, with no previous evidence of capillary

stagnation, an adequate capillary flow being maintained to within five to ten minutes of death. In the morphine group, spontaneous collapse occurred in 60 per cent of the animals. Omental blood flow in these showed only a moderate slowing to within fifteen to twenty minutes of death.

Vasomotion Following Hemorrhage.—Fig. 4 presents diagrammatically the changes in vasomotion following bleeding with the use of various anesthetic procedures. The phenomenon of vasomotion in the capillary circulation is the counterpart of vasoconstriction in the larger peripheral blood vessels. Both mechanisms appear almost simultaneously following hemorrhage. In this study the degree of narcosis utilized had no demonstrable effects on the vasoconstriction of the larger omental blood vessels. However, the different anesthetic agents did modify the amount of vasomotion prior to and following hemorrhage.

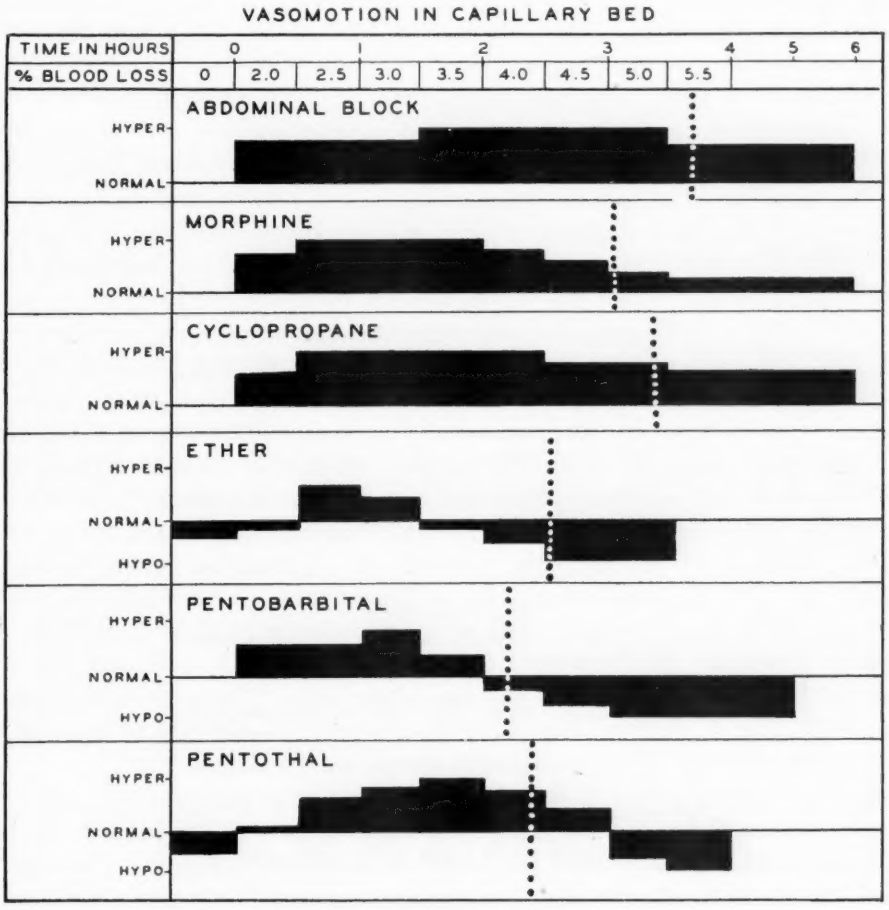

Fig. 4.—Dotted vertical lines indicate final bleeding.

In the control group, vasomotion recurred periodically at approximately one- to three-minute intervals. Within five to ten minutes following a 2 per cent blood loss, the constrictor phase of vasomotion began to predominate. Within twenty minutes its periodicity had increased to about one cycle every twenty seconds. This type of activity persisted throughout the experiment, that of the precapillaries becoming especially prominent. As a result, a continuous blood flow was restricted chiefly to the metarterioles and the central channels connecting them directly with the venules. The capillaries, most of which arise as side branches of these central channels, revealed only a sporadic, intermittent flow.

In the members of the group subjected to cyclopropane, an augmented vasomotion became evident soon after the onset of bleeding and, as in the controls, this activity was maintained throughout the period of observation. Dogs given morphine rapidly developed, after bleeding, an augmented vasomotion, which then decreased gradually and returned to its original level soon after maximal blood loss was reached.

The group receiving pentobarbital showed first a progressive increase and then a slow decrease in vasomotion over a three-hour period. Within thirty minutes after maximal blood loss was reached, vasomotion had disappeared completely. As previously mentioned, pentothal and ether anesthesia dampened vasomotion even prior to hemorrhage. When pentothal was used, vasomotion did not increase to the extent noted in the control group until a blood loss of approximately 3.5 per cent had been attained. It was then maintained at a high level until just following maximal blood loss, at which time it deteriorated rapidly and disappeared completely within forty-five minutes. Blood loss during ether anesthesia resulted in a moderate increase in vasomotion for about sixty minutes. Vasomotion then fell progressively to subnormal levels, being completely absent approximately twenty minutes after the last bleeding.

The persistence of active vasomotion was closely related to the maintenance of an adequate capillary circulation. When the blood flow was slowed sufficiently to impair the venous outflow from the capillary bed, vasomotion rapidly disappeared. The loss of vasomotion occurred earliest during pentothal and ether anesthesia. In the pentobarbital group, its loss was more gradual. Dogs given morphine did not develop a slowed blood flow to the degree obtained with ether, pentothal, or pentobarbital, and never completely lost their vasomotion. In the control and cyclopropane groups, in which capillary flow remained adequate, an augmented vasomotion persisted throughout.

Epinephrine Reactivity Following Hemorrhage.—An attempt was made to quantitate changes in the peripheral vascular bed during hemorrhage by studying the response of its muscular components to minimal concentrations of epinephrine. During hemorrhage the peripheral muscular components reacted to progressively smaller concentrations of epinephrine, topically applied. The increased reactivity was evidenced both by a response to extremely low dilutions and by a longer and more intense constriction. The significant feature, as noted in Fig. 5, was not the actual increment in reactivity to epinephrine but the persistence of this response with increasing blood loss.

In the control group, hemorrhage resulted in a progressive increase in epinephrine reactivity from a concentration of 1 part in 5 million to as high as 1 part in 50 million. Dogs given morphine closely resembled the controls except that their reactivity after hemorrhage increased only sixfold as against tenfold in the controls. Cyclopropane and pentothal brought about the largest proportional increase in reactivity following hemorrhage, despite the fact that the initial values prior to blood loss were two to three times higher than those of the controls. Dogs receiving pentothal showed an abrupt, rapid decrease in their epinephrine response. This occurred soon after maximal blood loss and a marked slowing in capillary flow, as noted in Fig. 3. In contrast, during cyclopropane anesthesia, where capillary blood flow remained adequate, the reactivity was maintained throughout. The ether and pentobarbital groups exhibited a progressive decrease in epinephrine response in the interval after the last bleeding.

In general, a decreasing epinephrine reactivity occurred in the same animals which showed a decreasing vasomotion, although the two processes did

not closely parallel each other. When both criteria were subnormal, the prognosis for recovery was poor. Infusion at this time resulted in a relaxation of the larger arteries and a passive dilatation of the muscular components of the capillary bed.

Analysis of Blood Samples.—The omental circulatory criteria were correlated with changes in venous oxygen, blood uric acid, and the presence of vasoexcitors and vasodepressors in the blood.

Venous oxygen: The normal values listed in volumes per cent in Table I varied somewhat with the anesthetic procedure, being lowest in the morphine and control groups, which received no oxygen. Therefore, for purposes of comparison, the venous oxygen data were considered as fractions of the normal, rather than as volumes per cent. This procedure was valid since there were no actual differences in any of the other criteria studied referable to the administration of oxygen.

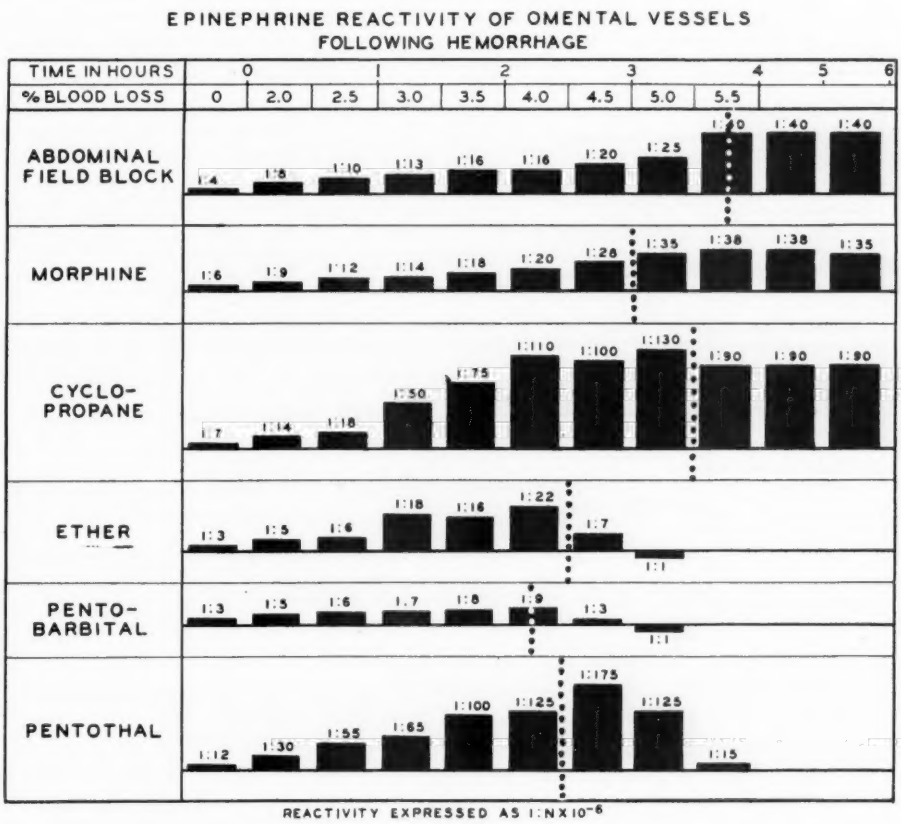

Fig. 5.—Minimal effective concentrations of epinephrine, topically applied, indicated as 1 :n × 10^8. Dotted vertical lines indicate final bleeding.

In all experiments, regardless of the anesthesia, as hemorrhage increased there was a progressive decrease in venous oxygen until, following maximal blood loss, an abrupt decrease to minimal values occurred. The gradual decrease reduced the oxygen to one-half to one-third its original value, and the ensuing abrupt decline brought it to one-eighth to one-tenth of normal. In actual volumes per cent, these critical values ranged from 1.5 to 3.5. Dogs falling below this level invariably died. The point in the syndrome at which the abrupt fall in venous oxygen occurred, followed by a variable period (ten to forty minutes) the onset of capillary stagnation in the omentum. No evi-

dent relationship was found between the level of venous oxygen and the deterioration of vasomotion and epinephrine reactivity.

Blood uric acid: As noted in Table I, the normal uric acid values in all experiments ranged from 0.8 to 2.1 mg. per cent. The highest values were obtained during pentobarbital anesthesia, in which the uric acid increased from 1.0 to 4.5 to 4.7 mg. per cent, a four- to fivefold increase. In all other groups, the uric acid levels increased two- or threefold, reaching 2.4 to 3.5 mg. per cent following hemorrhage. As a rule, the largest proportionate increase in uric acid was obtained in those animals which became refractory to transfusion, that is, those given pentothal, pentobarbital, and ether. The smallest

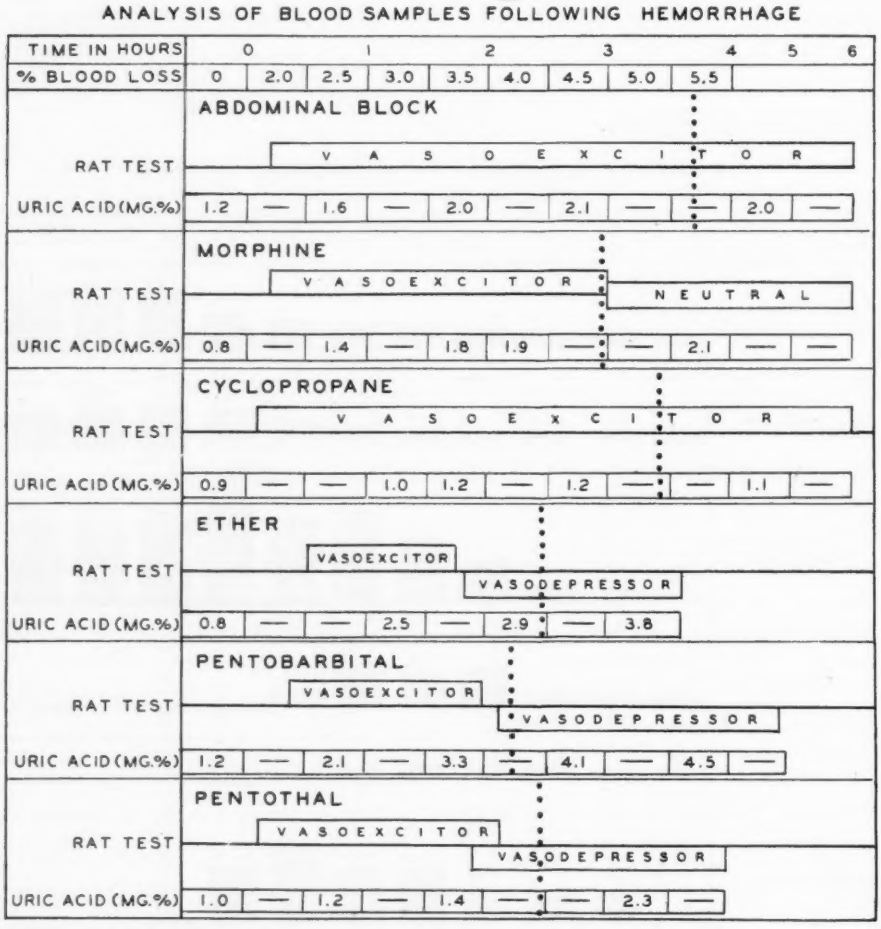

Fig. 6.—Presence of vasoexcitor and vasodepressor substances in blood samples. Blood uric acid values are average figures.

relative increase occurred in the cyclopropane and control groups. Dogs receiving morphine showed an intermediate increase in blood uric acid values. It should be noted that blood uric acid levels rose most in those instances in which the omental circulation was poorest, increasing progressively as peripheral blood flow slowed. The only positive correlation between blood uric acid levels and other criteria studied was found to exist in dogs whose blood samples exhibited vasodepressor properties. As indicated in Fig. 6, such dogs invariably showed the highest uric acid levels.

Rat Mesoappendix Test for Vasoexcitors and Vasodepressors in Blood.—In conjunction with a previous general study of changes in the peripheral circulation in the shock syndrome, a test was devised for the detection of reactive

substances in the blood stream.[8] This earlier study revealed the presence of "toxic" substances in the blood of dogs subjected, during morphine or pentobarbital anesthesia, to hemorrhage graded so as to induce a state in which the animal became irreversible to infusions of previously lost blood. The rat mesoappendix test was performed by the intravenous injection of 0.5 c.c. of heparinized plasma or serum derived from blood samples, removed at intervals during the experiment. Samples from unbled dogs had no effect on the capillary circulation of the rat mesoappendix other than a transient speeding of blood flow. Samples withdrawn after hemorrhage reproduced in the circulation of the test rat changes similar to those observed in the omentum of the shocked dog. Vasoexcitor substances were associated with the initial blood loss and vasodepressors appeared when the omental circulation evidenced deterioration.[8]

Similar tests on the rat mesoappendix were performed in this series (Fig. 6). When injected into the test rat, blood samples from animals in the control group gave vasoexcitor responses in the mesoappendix. This effect appeared soon after the first bleeding, and persisted throughout the experiment. No vasodepressor response was obtained, even in the three dogs that died. The rat mesoappendix responded in essentially the same manner to blood samples from dogs given cyclopropane. In the morphine group, vasoexcitor responses were elicited by samples taken shortly after initial blood loss. This type of reaction was obtained until the blood loss reached 3.5 per cent, after which the blood samples became nonreactive or neutral. In the previously reported study,[8] vasodepressors did appear in the blood of dogs given morphine, after they had been maintained in extreme hypotension (40 to 45 mm.) by support with repeated small infusions. Results in the pentobarbital groups were essentially the same as previously reported. Vasodepressors appeared within forty-five to ninety minutes after maximal blood loss was reached. Dogs during ether anesthesia showed the earliest appearance of vasodepressor in the blood, fifteen to twenty minutes after a 2.5 to 3.0 per cent blood loss. Samples from dogs receiving pentothal elicited the most pronounced vasoexcitor response. Vasodepressor reactions appeared suddenly after the hemorrhage had reached 3.5 per cent. As a result, blood samples taken thirty to forty minutes after maximal blood loss showed the presence of both vasoexcitors and vasodepressors. In instances where pentothal animals did not collapse until two hours after maximal blood loss, blood samples taken just prior to collapse produced only vasodepressor responses. In general, it was observed that vasodepressors appeared in the blood about the time that the omental circulation began to deteriorate.

DISCUSSION

An adequate evaluation of the factors operating in the shock syndrome must of necessity take into account the changes introduced by anesthesia, a hitherto neglected variable. This is especially true in comparing data of experiments carried out during different types of anesthesia. Even though a considerable portion of the experimental work in general has been on animals receiving barbiturate anesthesia, standardization is not possible since the barbiturates differ in their pharmacologic action, in the duration of their activity, and in the site and rate of detoxification. Previous attempts to evaluate the influence of certain anesthetic agents in shock[9, 14-17] did not use criteria which were sufficiently accurate indices of the progressive nature of the syndrome.

This feature has been overcome, to a considerable degree, in the present study by the utilization of characteristic changes in the activity of the capillary bed, a portion of the vascular tree directly involved in the circulatory collapse.

The present study has shown that dogs subjected to a controllable and standardized type of hemorrhage present well-defined differences in their circulatory reactions, depending upon the anesthetic agent used. Objective evidence for this was obtained by employing the peripheral circulation of the omentum as a criterion. Had emphasis been placed solely on the other criteria presented, clear-cut evidence would not have been available until the terminal phases of the syndrome had been reached.

Omental blood flow was the single criterion which could be used by itself to evaluate the general status of the animal at any stage in the syndrome. The rate of flow alone provided an excellent visual prognostic guide. In addition, a critical estimate of the basic features underlying peripheral circulatory failure was obtained by recording changes in the functional integrity of peripheral vascular mechanisms. These mechanisms include vasomotion, reactivity of the muscular elements, patterns of distribution of blood flow through the capillary bed, degree of constriction in the arteries feeding the bed, state of tone of the venous vessels, and adequacy of the venous outflow from the bed.

As a basis for comparing the influence of different anesthetic agents, use was made of the circulatory changes in animals regarded as unanesthetized controls, their only anesthesia consisting of local infiltration of procaine. These changes were remarkably uniform and proved to be an especially satisfactory set of controls. Bleeding, in these animals, resulted in a compensatory vasoconstriction of the larger omental arteries and the development of increased vasomotion in the capillary bed. This hyper-reactive state persisted for a period of five to six hours, at which time the dogs were sacrificed.

Each of the anesthetic agents investigated produced variations from the controls in one or more of the criteria studied. Cyclopropane produced the least change in the peripheral circulatory dynamics. In addition, it was the only anesthetic agent which resembled the controls in maintaining a high level of peripheral compensatory reactivity throughout. It was significant that the controls and those receiving cyclopropane gave evidence of the least decrease in the efficiency of the peripheral circulation, showed the lowest experimental mortality, had the longest survival time, tolerated greatest hemorrhage, and responded best to replacement of lost blood.

Evans[18] in a recent publication states that the preferred anesthesia in shock is local procaine block or cyclopropane. An experimental study on dogs (using a thermocouple flowmeter) by Bennett, Bassett, and Beecher[4] found, on a basis of changes in flow and blood pressure in the major blood vessels, that cyclopropane offered a wider margin of safety after hemorrhage than evipal or ether. The present study has presented further objective evidence for the value of cyclopropane anesthesia in hemorrhage by demonstrating that, of all the anesthetic agents used, it produces the least deleterious change in the peripheral circulation.

Morphine, in the dose used, produced sedation but not complete anesthesia. This small dose brought about circulatory changes differing from those of the controls, especially a gradual decrease in capillary blood flow as maximal blood loss was attained. Although most of the morphine group was reversible to transfusion, the condition of the circulation at the end of the experiment was poorer than that of the controls. Blalock[19] offered evidence that unanes-

thetized dogs and those receiving 1 mg. per kilogram of morphine sulfate had similar bleeding volumes. In the present study, dogs receiving morphine (2 mg. per kilogram) resembled the controls only prior to hemorrhage and during moderate bleeding (< 3 per cent). When the dogs were bled more severely and maintained in extreme hypotension for an extended period (> 4 hours) they showed significant variations from the controls.

The barbiturates and ether were least satisfactory from several points of view. The dogs receiving these drugs uniformly showed a markedly reduced blood flow as bleeding progressed. In addition to the mechanical slowing of flow through the omentum, they showed a deterioration in the functional activity of the capillary bed. Such changes occurred while blood pressures were still relatively high. Dogs given ether or a barbiturate tolerated the least blood loss, had the shortest survival time, the greatest experimental mortality, and the poorest response to transfusion. Furthermore, they were the only groups to show the presence of vasodepressors in the blood, a feature previously reported to be associated with irreversibility to transfusion.[8]

Seeley, Essex, and Mann,[15] Kendrick,[16] Beecher, McCarrell, and Evans,[9] and Pender and Essex,[17] in studies of shock time, death time, and hemoconcentration during anesthesia with various barbiturates and ether, pointed out that the barbiturates were less deleterious than ether. The differences induced by various anesthetic agents, as established in the present study, confirm the observations of these authors on the barbiturates and ether. However, the present data indicate that, relative to the six anesthetic procedures studied, the effects of the barbiturates on the peripheral circulation do not compare favorably with local, cyclopropane, or morphine anesthesia.

In view of the marked differences introduced by the various anesthetic procedures, it was especially noteworthy that changes in blood pressure showed such poor correlation with any of the other criteria. The hazard of employing blood pressure levels as an index of the condition of the animal was further emphasized by the wide discrepancy between the critical blood pressure levels with different types of anesthesia. Blood pressures of 80 to 85 mm. in the control, cyclopropane, and morphine groups were associated with a good peripheral circulation and comparatively healthy state of the dogs, while the same blood pressure range in the pentothal and ether groups was associated with poor peripheral circulation and incipient collapse. Moon and associates[20] used a depressed mean blood pressure of 70 mm. to indicate the onset of shock. Beecher, McCarrell, and Evans,[9] in their report on the influence of anesthesia on experimentally induced hemorrhage in dogs, likewise used blood pressures of 70 mm. or below to designate the onset of shock. In the present study, this level corresponded to the critical blood pressure level of the ether group. With pentobarbital, a blood pressure of 70 mm. indicated a shock state in only a small percentage of the animals. Furthermore, as has been pointed out, in dogs subjected to procaine (local), cyclopropane, or morphine this blood pressure level did not indicate a shocked state.

The present experiments, by avoiding the introduction of many uncontrollable factors, sharply brought out the differences that could be attributed to anesthetic agents alone. Traumatic methods are difficult to control and to standardize because of the multiplicity of factors involved. On the other hand, hemorrhage, carefully guided by simultaneous observations of peripheral blood flow, provided a sensitive test method for evaluating both the shock syndrome and the effects due to anesthesia.

Pender and Essex[17] reported a comparative study of traumatic shock during ether, pentobarbital, and pentothal anesthesia. Their results, based on hemoconcentration, blood pressure, and survival time, indicate that pentobarbital is least deleterious, pentothal next, and ether considerably the worst. In the present study, with blood loss up to 3 per cent of the body weight, dogs receiving pentothal favorably resembled the controls, except for an early depression of vasomotion. With a more severe hemorrhage, however, these dogs showed a rapid deterioration of the peripheral circulation as marked as that of dogs receiving ether. Both these groups ultimately showed the severest disruption of the peripheral circulation and proved to be the most difficult to recover with transfusion. Although dogs in the ether group showed circulatory disturbances earlier, they did not deteriorate as rapidly as dogs in the pentobarbital or pentothal groups. Terminally, there was little difference among these three anesthetic procedures.

Beecher, McCarrell, and Evans[9] and Pender and Essex[17] pointed out that the administration of oxygen throughout their experiments resulted in no obvious differences between dogs which received oxygen and those which did not. Findings in the present study demonstrate no differences in the circulatory criteria after blood loss, although the administration of oxygen considerably elevated venous oxygen content.

Use of the described bleeding technique resulted in the spontaneous collapse of a definite percentage of dogs in each group. The majority of the dogs subjected to ether, pentobarbital, and pentothal anesthesia collapsed spontaneously within five to six hours. Their collapse was accompanied by a profound alteration of the peripheral circulation and by the appearance of vasodepressors in the blood. The lowest mortality occurred in the control and cyclopropane series. Mortality was slightly higher with morphine. All of these deaths occurred abruptly, with no previous disruption of the omental circulation and with no evidence of vasodepressor substances in the blood. It is therefore suggested that the barbiturates and ether predispose the dogs to circulatory collapse which may be due to the introduction into the blood stream of vasodepressor substances that interfere with the normal functional activity of the muscular components of the capillary bed.

SUMMARY

Peripheral circulatory studies were made on dogs subjected to a standardized bleeding procedure during six different anesthetic procedures: procaine (local infiltration), morphine sulfate, cyclopropane, ether, pentobarbital, pentothal.

1. *Blood Loss.*—Dogs subjected to local or cyclopropane anesthesia tolerated the greatest blood loss. Those given barbiturates withstood the least.

2. *Blood Pressure.*—Blood pressure levels following equivalent blood loss differed considerably with each anesthetic agent and were found to be the least reliable of the circulatory criteria used.

3. *Blood Flow.*—Blood flow reflected most accurately the general condition of the animal. The most efficient blood flow after hemorrhage occurred in dogs subjected to local or cyclopropane anesthesia. Dogs given ether showed the poorest blood flow after hemorrhage.

4. *Vasomotion.*—After hemorrhage, vasomotion, a functional aspect of the peripheral circulation, was maintained in an augmented state in dogs given procaine, cyclopropane, or morphine. It was depressed by pentothal and ether.

5. *Epinephrine Reactivity.*—Dogs receiving local or cyclopropane anesthesia maintained the hyper-reactivity which developed after the initial bleeding. With the other anesthetic agents the epinephrine response became subnormal, dogs given pentobarbital, morphine, and ether showing a gradual decrement and those given pentothal an abrupt fall.

6. *Venous Oxygen.*—Venous oxygen fell in all the cases.

7. *Blood Uric Acid.*—Blood uric acid showed a gradual increment in all instances, being greatest in those dogs irreversible to transfusion.

8. *Rat Mesoappendix Test.*—Vasodepressors were found after hemorrhage in the blood of dogs given ether, pentobarbital, and pentothal.

CONCLUSION

The peripheral circulatory dynamics in dogs subjected to cyclopropane anesthesia were found to approach most closely those of controls receiving local anesthesia. The use of barbiturates and of ether resulted in marked deviations from the controls and the development of a state refractory to blood replacement therapy.

We are indebted to Mr. L. Dziorney for his valuable technical assistance.

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PULSION DIVERTICULUM OF THE HYPOPHARYNX AT THE PHARYNGO-ESOPHAGEAL JUNCTION

Surgical Treatment in 140 Cases*

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THE occurrence of a diverticulum at the pharyngo-esophageal junction which obstructed deglutition was first observed by Ludlow[1] in 1767. Since that time this condition has been of considerable general interest to anatomists, physiologists, clinicians and roentgenologists, and particularly to surgeons, since operative treatment is the only treatment that will correct the condition and relieve its symptoms.

A diverticulum can occur in any part of the pharynx and esophagus. Since Rokitansky's[2] description of traction diverticula in 1840, they have been classified into two general types: pulsion diverticula and traction diverticula. Pulsion diverticula are most commonly situated in the hypopharynx close to the junction of the pharynx and the esophagus and are often termed "pharyngo-esophageal diverticula." This term probably is incorrect from a strictly anatomic standpoint, for two reasons: (1) Since this abnormality rarely has a muscular coat, it is not a true diverticulum and may be more correctly termed a "saceulation." (2) It is essentially a herniation of the mucous membrane through the muscular wall of the pharynx and not through the wall of the esophagus. However, since the site is close to the pharyngo-esophageal junction and since most of the symptoms are referable to the esophagus, the term "pharyngo-esophageal diverticulum" is very descriptive. The term "pharyngeal diverticulum" should be reserved for those rare lesions that occur in other parts of the pharynx. Pulsion diverticula also occasionally develop in the lower esophagus just above the diaphragm. The diverticulum that occurs most frequently in the esophagus, however, is the traction type and its most common site is the middle third of the esophagus. Esophageal diverticula will not be considered in this paper.

The site of origin of pulsion diverticula at the pharyngo-esophageal junction has been the subject of much discussion and considerable difference of opinion as to whether they originate in one or more regions. Maes and McFetridge[3] stated that they always occur at the same point in the posterior wall of the pharynx directly back of the cricoid cartilage at the junction of the pharynx and the esophagus. Lahey[4] stated that they occur at two points through the mid-posterior wall of the pharynx: (1) through a region beneath the lowest fibers of the inferior constrictor muscle and (2) at the pharyngo-esophageal dimple, the defect in the posterior wall where the cricopharyngeus muscles diverge from the lowest fibers of the inferior constrictor muscle. Shallow[5] gave three sites of origin, the first being the most common: (1) the commonly described area above the cricopharyngeus muscle either on the right or left side, more frequently on the left, (2) the Killian-Jamison region on the posterolateral wall of the pharynx below the cricopharyngeus muscle and above the circular fibers of the esophagus, and (3) through the lower portion of the inferior constrictor muscle.

Received for publication, March 16, 1945.
*Read at the meeting of the Western Surgical Association, Chicago, Ill., Dec. 1-2, 1944.
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I have had the opportunity of studying six specimens removed at necropsy in cases in which the patients died of other causes. The opening in three instances was through a defect in the left posterolateral wall of the pharynx between the inferior constrictor and cricopharyngeus muscles. In one instance the opening was in a similar position on the right side and in two the opening was posterior through the lower fibers of the cricopharyngeus muscle above the esophagus. Three of these specimens, each showing one of the three different sites of origin of the diverticulum, are shown in Fig. 1.

Determination at operation of the exact site of origin of a diverticulum passing through the muscular wall of the pharynx often is difficult, particularly if the diverticulum is large and has a large opening. However, the origin of smaller ones can be established fairly accurately. In the 140 cases in which I have operated, diverticula were found in four different regions in the posterior

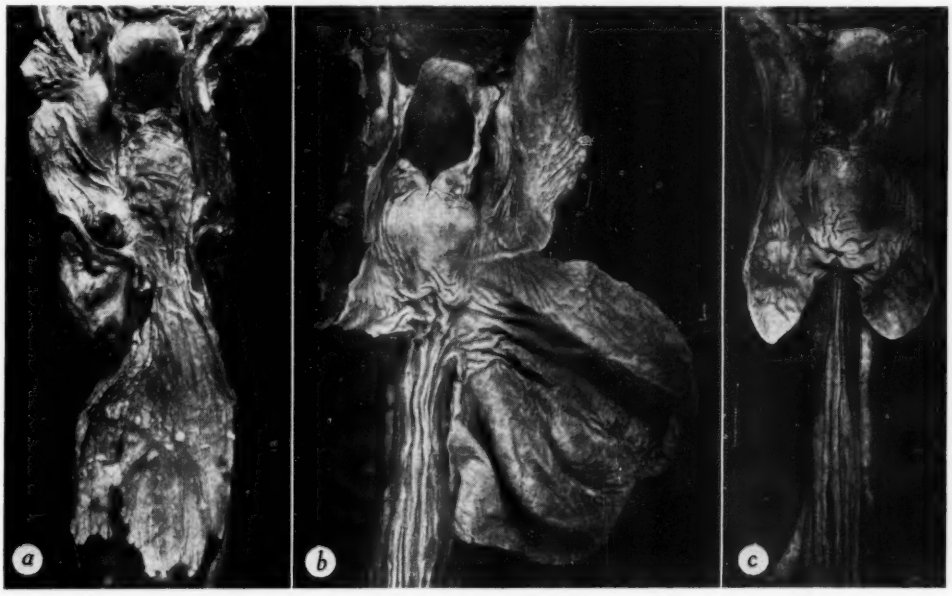

Fig. 1.—*a*, Diverticulum originating from the left posterolateral wall of the pharynx with the opening between the inferior constrictor and the cricopharyngeus muscle. *b*, Diverticulum originating from the right posterolateral wall of the pharynx with the opening between the inferior constrictor and the cricopharyngeus muscle. *c*, Median type of diverticulum originating from the posterior wall of the pharynx between the inferior constrictor and the cricopharyngeus muscle.

and lateral pharyngeal walls, as follows: (1) left posterolateral wall between the inferior constrictor and cricopharyngeus muscles, (2) right posterolateral wall between the inferior constrictor and cricopharyngeus muscles, (3) midline, posterior wall, beneath the median raphe of the inferior constrictor muscle and above the cricopharyngeus muscle, and (4) midline, posterior wall, through or immediately beneath the cricopharyngeus muscle above the esophagus (Figs. 2, 3, and 4).

In one case in this series there were two diverticula. One, which was of moderate size, originated from the left posterolateral wall between the inferior constrictor and cricopharyngeus muscles, and the other, a smaller diverticulum, originated from the right posterolateral wall of the pharynx.

There is considerable difference of opinion as to the cause of pharyngoesophageal diverticula.

Their fairly constant location suggests congenital origin, although they usually do not occur in more than one member of a family. In the 140 cases

in which I have operated, a diverticulum in another member of the family was noted only twice. In one instance the patients were mother and son, and in the other, father and son.

The uniform relationship of the cricopharyngeus muscle to the site of herniation suggests that some congenital malformation of the attachments of this muscle may be a causative factor. The cricopharyngeus muscle, which is attached to the cricoid cartilage anteriorly by an elastic aponeurosis, is the chief closing muscle of the esophageal opening. If some malformation of this muscle exists, it may perform its function satisfactorily during early life. However, the elastic tissue attachments weaken with abnormal stress and atrophy of increasing years, and a herniation may develop as the result of constant and increasing pressure on this congenitally weak region. The foregoing theory was suggested by the average age of patients of this series, which is 57 years.

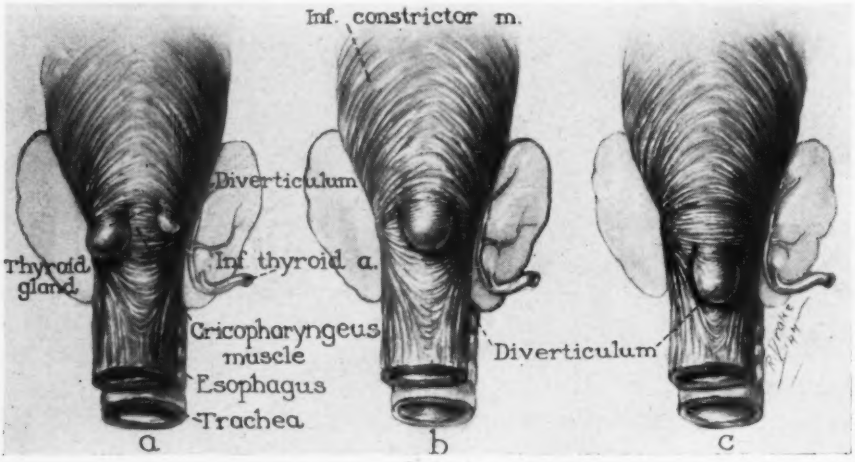

Fig. 2.—Four sites of origin of pharyngo-esophageal diverticula as found at operation: (1) left posterolateral wall between the inferior constrictor and the cricopharyngeus muscle; (2) right posterolateral wall between the inferior constrictor and the cricopharyngeus muscle (1 and 2 shown in *a*); (3) midline, posterior wall, beneath the median raphe of the inferior constrictor muscle and above the cricopharyngeus muscle (shown in *b*); (4) midline, posterior wall, through or immediately beneath the cricopharyngeus muscle above the esophagus (shown in *c*).

In respect to the average age of patients and cause, pharyngo-esophageal diverticula are somewhat analogous to diaphragmatic hernias through the esophageal hiatus. The average age of patients who have a diaphragmatic hernia through the esophageal hiatus is 55 years. These hernias may be caused by atrophy of the diaphragmatico-esophageal membrane which is an elastic tissue aponeurosis that compensates for a congenitally large esophageal hiatus until it atrophies from increasing age and stress.

Many other theories have been advanced to explain the cause of pharyngo-esophageal diverticula. These theories include neuromuscular in-co-ordination during the act of swallowing; a physiologic basis, that is, increased pressure on the posterior wall of the pharynx; and muscular deficiency at the points of entrance of nerves and blood and lymphatic vessels through the muscles of the posterior wall of the pharynx. It is probable that muscular deficiency is the predisposing cause and that other factors are the inciting element. This would tend to explain why the symptoms are progressive and usually do not present definite form until the patient has reached middle age.

In this series of 140 cases, 107 patients were men and 33 were women. The ages of the patients varied greatly, the oldest being 80 years of age and the youngest being 34. The average age was 57 years. Seven patients were between

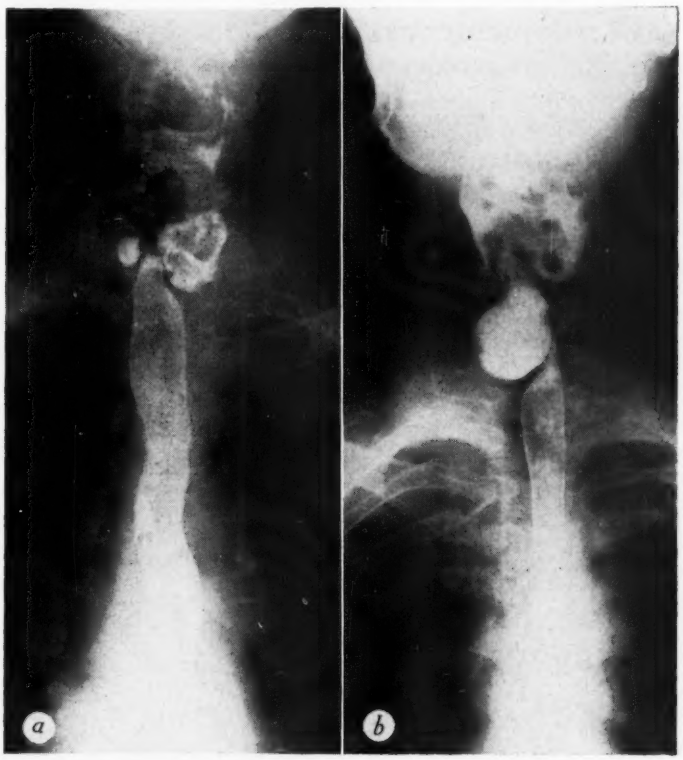

Fig. 3.—*a*, Two diverticula, one from the left and one from the right posterior wall of pharynx. The left diverticulum, which originated between the inferior constrictor and the cricopharyngeus muscle, was removed by a one-stage operation through a left cervical approach. The small diverticulum on the right was not removed. *b*, Diverticulum in the right posterolateral wall, originating between the inferior constrictor and the cricopharyngeus muscle, removed by one-stage diverticulectomy through right cervical approach.

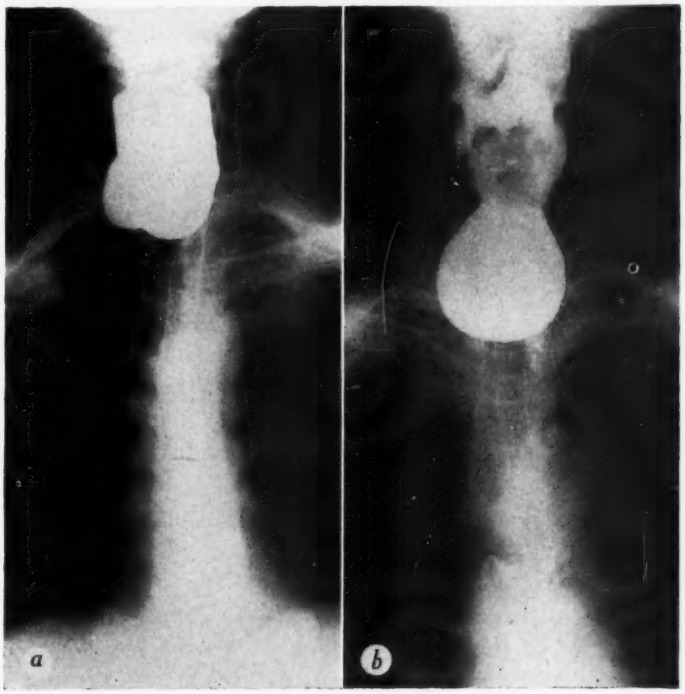

Fig. 4.—*a*, Large median diverticulum originating beneath the median raphe of the inferior constrictor muscle posteriorly, removed by one-stage diverticulectomy through left cervical approach. *b*, Large median type diverticulum extending into mediastinum and originating through the lower fibers of the cricopharyngeus muscle above the esophagus, removed by one-stage diverticulectomy through left cervical approach.

the ages of 30 and 39 years; twenty-five between 40 and 49 years; fifty-seven between 50 and 59 years; thirty-eight between 60 and 69 years; eleven between 70 and 79 years, and two patients were 80 years of age.

CLINICAL MANIFESTATIONS

The clinical manifestations of pharyngo-esophageal diverticula vary as to type, duration, progress, and severity. The symptoms are progressive, depending on the type of sacculation as well as on the rapidity with which it increases in size (Fig. 5).

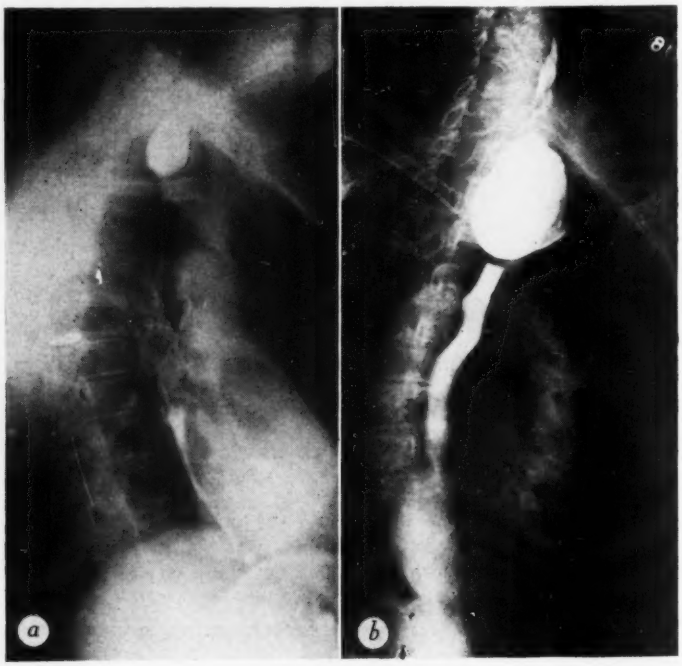

Fig. 5.—Progressive development of pharyngo-esophageal diverticulum. *a*, First admission, 1927: moderate-sized diverticulum causing moderate symptoms. Patient refused operation. *b*, Second admission, 1936: diverticulum had increased about three times in size in the intervening nine years, causing symptoms of retention of food and partial obstruction of the esophagus. Patient consented to operation.

In 80 per cent of the 140 cases in this series the symptoms were vague and indefinite at onset and were slowly progressive. In 20 per cent of cases the symptoms were more rapid in progress and severity. The duration of symptoms was from one to twenty-five years, the average duration before operation being approximately five years. This difference in the rate of progress of symptoms is more related to the character of the neck than to the size of the sac. In many instances a relatively small diverticulum which has a small opening produces disabling symptoms, whereas a large diverticulum which has a large opening produces relatively little distress and disability because the contents of the sac can be more easily emptied. However, regardless of the size of the opening, the severity of the symptoms increases with the size of the diverticulum, particularly after it becomes large enough to retain food and secretions. Ultimately, complete esophageal obstruction may result. In this series, fifteen patients had marked obstruction and three had complete obstruction at the time of admission to the clinic. In one of the latter patients, it was necessary to perform a preliminary gastrostomy for feeding but in the others it was possible to pass an indwelling stomach tube for preoperative feeding (Figs. 6 and 7).

The earliest symptom usually is dysphagia. There is a sensation of a foreign body obstructing the normal process of swallowing and food seems to stick in the

throat. Later, food and mucus are regurgitated. These symptoms do not occur until a definite sacculation is formed. Noisy deglutition and gurgling sounds in the throat, which result from the swallowing of air and the accumulation of food and mucus in the sac, often occur. If there is difficulty in regurgitating the food, pressure on the side of the neck will often aid in emptying the sac.

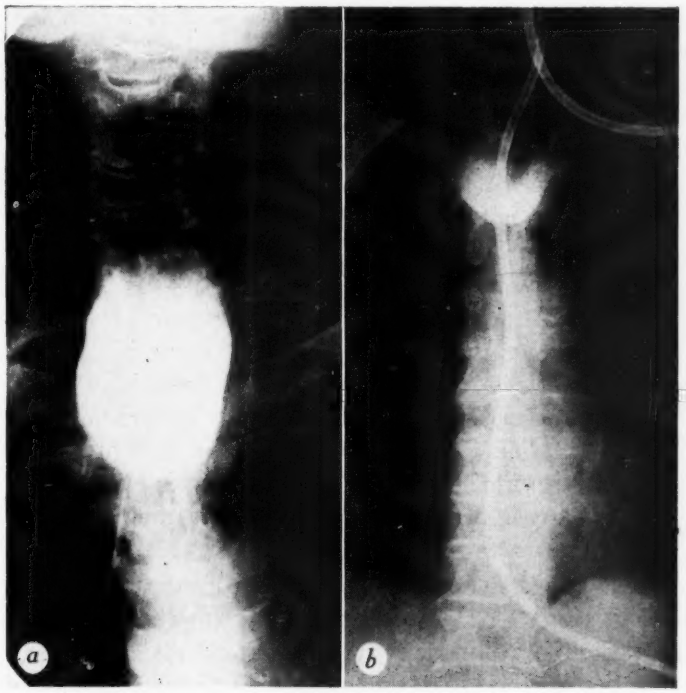

Fig. 6.—Pharyngo-esophageal diverticulum, median type, originating below the cricopharyngeus muscle, causing complete obstruction. Patient 80 years of age. Weight loss twenty-five pounds (11 kg.). *a*, Diverticulum extending into mid-mediastinum. *b*, Three days later, after introduction of indwelling stomach tube for feeding; residual barium in diverticulum.

Fig. 7.—*a* and *b*. Nineteen days after one-stage diverticulectomy. Left cervical approach; esophagus normal, incision healed.

After the sac has become well developed, its enlargement is more rapid than before because of the increased pressure from within, which is caused by the more or less constant retention of food and secretions. The sac pushes downward and backward, between the prevertebral and the pretracheal fascia, into the mediastinum, and may extend to the arch of the aorta. Progressive esophageal obstruction often occurs because the enlarging opening of the diverticulum is pulled downward and forward and obstructs the normal esophageal orifice. This orifice, which often becomes a narrow slit, may be pushed laterally. The portion of the upper part of the esophagus that is in apposition to the diverticulum is flattened and distorted by direct pressure of the body of the sac. Food enters the diverticulum first and then overflows into the esophagus. Patients often spend hours at their meals in order ot obtain enough nourishment to sustain life. The loss of weight may be great, one patient in this series having lost 100 pounds (45.4 kg.) before admission to the clinic.

The largest sac found in this series filled the entire superior mediastinum and extended into the right thoracic cavity. After its removal it held 825 c.c. of fluid. This patient had had symptoms for fifteen years. For the last year he had had marked retention of food in the diverticulum with increasing difficulty in taking solid food. His diet had consisted chiefly of milk. Before he could get any food into the esophagus, he had to drink more than one pint of milk. He reported that he ate and regurgitated food three or four times at a meal before he was successful in getting any appreciable amount of food into the esophagus. He had lost twenty-five pounds in the last three months.

When a large sac that extends into the mediastinum is filled with food it produces marked pressure on the adjacent intrathoracic organs and causes a distressing sensation of fullness in the thorax, which often is associated with dyspnea, palpitation of the heart, and a sense of suffocation. Severe cough and choking spells frequently occur. Many times patients lower their heads, as is customary in postural drainage, and then press on the side of the neck in order to empty the sac. In some instances food may enter the trachea and cause marked cyanosis.

Repeated aspiration of food into the bronchi may result in bronchitis or bronchiectasis. In this series of 140 cases, bronchitis was present in nine cases, and bronchiectasis in four. Associated hoarseness of the voice also occurs. This is caused by pressure or inflammatory reaction around the recurrent laryngeal nerve, which is often close to the neck of the sac. In this series of cases, hoarseness was present in eight cases; the vocal cord was fixed in two cases.

After the sac has become definitely formed, the symptoms are definite and characteristic. The diagnosis usually can be made on the basis of the symptoms, but it should be proved by roentgenographic examination. In the earlier stages when the symptoms are vague, a definite clinical diagnosis may not be possible without an esophagoscopic or roentgenologic examination. These methods are the most accurate in the establishment of a definite diagnosis and they should be employed in all cases in which there are any persistent signs of dysphagia. The longer the diagnosis is delayed, the greater is the risk of serious complications which may enhance the difficulties and may impair the results of surgical treatment.

TREATMENT

Although pharyngo-esophageal diverticula first were recognized more than 175 years ago, they were not treated surgically until 1877, about sixty-eight years

ago, when Nicoladoni[6] produced a cervical fistula by diverticulotomy. This procedure obviously could not effect a cure. Neihans,[7] in 1884, reputedly was the first surgeon to perform a primary diverticulectomy but the operation was not successful. The first successful operation for the condition was reported by von Bergmann[8] in 1892. These early operations were associated with a relatively high mortality, chiefly because of mediastinitis, pneumonia, and pulmonary abscess. In many cases in which the patients recovered, the morbidity was great because of a pharyngeal fistula. These complications led to the operation in two stages, which Goldmann,[9] of Freiburg, is credited with introducing in 1909. This procedure greatly reduced the mortality.

Complete extirpation of the diverticulum by operative measures now is generally accepted as the only method of treatment that will completely relieve the symptoms. There is still some difference of opinion, however, as to whether diverticulectomy should be performed in one stage or in two stages. Both operative procedures are favored by various surgeons of wide experience. Lahey,[4] in 1940, reported a series of 118 cases in which the two-stage procedure was used. One patient died and three had recurrences that required reoperation. Shallow,[5] in 1936, reported a series of seventy-nine cases. Seventy-six of these patients underwent a one-stage operation and three, a two-stage operation. There were two operative deaths and two recurrences.

In the 140 cases in which I have operated for pharyngo-esophageal diverticulum, both the one-stage and the two-stage procedures have been employed. This series includes the thirty-three cases which I[10] presented at the Forty-Seventh Annual Meeting of the Western Surgical Association, Dec. 3, 1937. The one-stage operation was performed in eight of the thirty-three cases and the two-stage operation in twenty-five. Since 1937, I have performed the one-stage operation in 107 additional cases. Thus, in this series of 140 cases, the one-stage operative procedure was performed in 115 cases and the two-stage procedure in twenty-five cases.

Complete removal of the sac, including its neck, is generally accepted as the only effectual surgical procedure for pharyngo-esophageal diverticulum. The technical difference in the two operative procedures advocated to accomplish this purpose is in treatment of the sac and the time of its removal. In the one-stage procedure the sac is removed at the primary operation. In the two-stage procedure a temporary diverticulopexy is performed and the sac is removed at a second operation seven to ten days later. The fundamental difference in these two procedures is that in the one-stage operation the fascial planes leading to the mediastinum are not walled off prior to removal of the diverticulum and in the two-stage operation the interval between the operations permits the formation of granulations which wall off the fascial planes of the neck and mediastinum.

Preoperative Considerations.—Patients who have lost considerable weight as a result of their inability to obtain sufficient nourishment require preoperative feeding. In most instances this can be accomplished by an indwelling stomach tube. Sixteen patients in this series of 140 cases were prepared for operation by this means. In one case in which complete obstruction was present it was impossible to pass the stomach tube, and a preliminary gastrostomy was necessary for feeding.

Dilatation of the introitus of the esophagus is advisable and has been performed routinely in the last fifty cases of this series. In many instances the

introitus is distorted and dilatation minimizes the danger of exerting pressure at the site of closure of the pharynx when the patient swallows food postoperatively.

In all cases in which there is any evidence of retention in the diverticula, roentgenologic study of the thorax should be performed immediately before operation. The reason for this is to be certain that no barium has been retained in the diverticulum which at operation might be aspirated into the lungs. In those cases in which retention exists, the diverticulum should be irrigated thoroughly to remove the contents.

The vocal cords should be checked both preoperatively and postoperatively. In any case in which the patient has symptoms of hoarseness it is particularly advisable to check the vocal cords preoperatively.

A thread which is passed through the esophagus into the stomach the night before operation is left in place until the patient is taking nourishment satisfactorily after operation. This provides a guide over which a stomach tube can be passed if a postoperative pharyngeal fistula should develop. This, however, may be unnecessary since only one of my patients has required passage of a stomach tube postoperatively because of a pharyngeal fistula. Formerly I left a stomach tube through the esophagus at the time of operation but this practice was discontinued because the tube was often irritating to the esophagus and produced considerable mucus which may be detrimental to healing of the pharynx.

Operation should not be undertaken if the patient has had a recent infection of the throat or lungs, because of the danger associated not only with infection of the throat but also with cough postoperatively, both of which would interfere with the healing of the tissues.

Anesthesia.—I prefer regional nerve block by the use of procaine. This method permits the patient's reflexes to remain active, which is a helpful safeguard in many instances. If an accumulation of secretions is present in the sac at operation, these secretions can be carefully emptied into the pharynx; they may be either aspirated by suction or swallowed. The act of swallowing is often helpful in identifying small diverticula as air is forced into the sac. The surgeon also finds it helpful if the patient can talk during dissection around the neck of the sac posteriorly, because of the close proximity of the recurrent laryngeal nerve. This is particularly true in those cases in which, because of considerable inflammatory reaction around the neck of the sac and in the surrounding tissues, visualization of the nerve is difficult.

Methods of Approach.—The method of approach to the diverticulum depends on its location but it should be from the side of the neck on which the diverticulum is situated. Diverticula usually occur on the left side but in many instances occur on the right side. In this series of 140 cases, the approach was through the left cervical region in 116 cases and through the right cervical region in 24 cases. In one case, an infected diverticulum was removed through the left cervical approach. The diverticulum subsequently recurred on the right side and the approach was through a right cervical incision.

The side of the neck from which to approach a diverticulum is determined by a careful study of the anteroposterior roentgenogram. In some instances in which determination of the exact position of the neck of the sac is difficult, esopnagoscopic examination is of value.

I should like to re-emphasize the importance of approaching diverticula which originate from the posterolateral wall of the pharynx from the side of the neck on which they are situated. This approach, I believe, is accompanied

by much less risk of injury to the surrounding structures, particularly the recurrent laryngeal nerve, than an approach from the opposite side. It greatly facilitates exposure of the neck of the sac so that it can be clearly visualized and separated from the surrounding muscles, and insures complete excision of the sac. In this way there is much less danger of leaving a residual spur or pouch which may result in recurrence. In those cases in which the diverticulum originates in the midline, I prefer a left cervical incision.

Operative Technique of One-Stage Operation.—Inasmuch as I now rarely, if ever, do the two-stage operation, having used the one-stage procedure in the last 112 consecutive cases, the technique of this procedure will not be discussed here. It was fully described in my presentation before the Western Surgical Association in 1937.

In the one-stage procedure the incision is made through the skin and platysma myoides muscle, and along the anterior border of the sternocleidomastoid muscle from the hyoid bone above to a point about 2 cm. above the clavicle. The external jugular vein is often in the line of incision; in these instances the vein is cut and ligated. The sternocleidomastoid muscle then is separated from the omohyoid and sternothyroid muscles. The latter are retracted medially. This exposes the carotid sheath which, with the sternomastoid muscle, is retracted outward. The thyroid gland is exposed and retracted upward and medially; this exposes the peritracheal fascia which surrounds the trachea and esophagus. If appreciable hypertrophy of the thyroid gland is present, partial lobectomy may be necessary in order to obtain adequate exposure of the fascial coverings of the diverticulum. In many instances, particularly if the diverticulum is approached from the right side, the inferior thyroid artery and vein course over the diverticulum and in these cases the vessels should be cut and ligated. The fascia then is incised posterior to the trachea at about the level of the cricoid cartilage. The neck of the diverticulum usually is located readily at a point opposite the level of the cricoid cartilage. Several methods, such as the use of bougies and the esophagoscope, have been suggested for locating the diverticulum but I have not found these methods necessary. There is never any difficulty in locating the larger types of diverticula as they lie lateral or posterior to the esophagus. The small diverticula, which often are buried in the cervical fascia, can be located readily by the simple procedure of having the patient swallow or force air into the diverticulum. The location of diverticula that occur through the posterolateral wall of the pharynx is greatly facilitated by approaching them from the side of the neck from which they originate. If a diverticulum originates from the right posterolateral wall of the pharynx and is approached from the left side, there may be considerable difficulty in locating it as well as in visualizing the neck of the sac.

After the diverticulum has been located, the fascial coverings are carefully dissected away until the true wall of the sac is reached (Fig. 8). The fundus of the sac is elevated into the wound and dissection of the neck of the sac is carried out as it appears through the muscular wall of the pharynx. Great care should be exercised in this dissection to avoid perforation of the sac or injury of the surrounding structures, particularly the recurrent laryngeal nerve. This nerve is often in close proximity to the neck of the sac, particularly in those cases in which the sacculation passes through or beneath the cricopharyngeus muscles. It is important not to separate the fascial planes more than necessary to remove the body of the sac, particularly when the diverticulum extends into the mediastinum.

After the sac has been completely dissected free from the surrounding structures, the true neck of the sac is dissected from the pharyngeal muscles. Particular care is taken to separate and remove any fibers of the inferior constrictor muscle and of the cricopharyngeus muscle above and beneath the neck of the sac, respectively. In many of the larger diverticula, the opening into the pharynx is large and consists essentially of diffuse bulging of the back wall of the pharynx. In this type, great care should be exerted to determine the true relationship of the opening of the sac to the muscular wall of the pharynx, which often is much thinned out. It is important to dissect these diffuse sacculations from the muscle and to establish as small a neck to the sac as possible, being careful not to remove too much of the mucous membrane because of the danger of producing a stricture. After the true neck of the sacculation has been isolated from the surrounding muscles, it is transfixed by the use of chromic catgut and the diverticulum is completely excised. The stump of the sac is then invaginated into the wall of the pharynx and the muscles of the wall which sur-

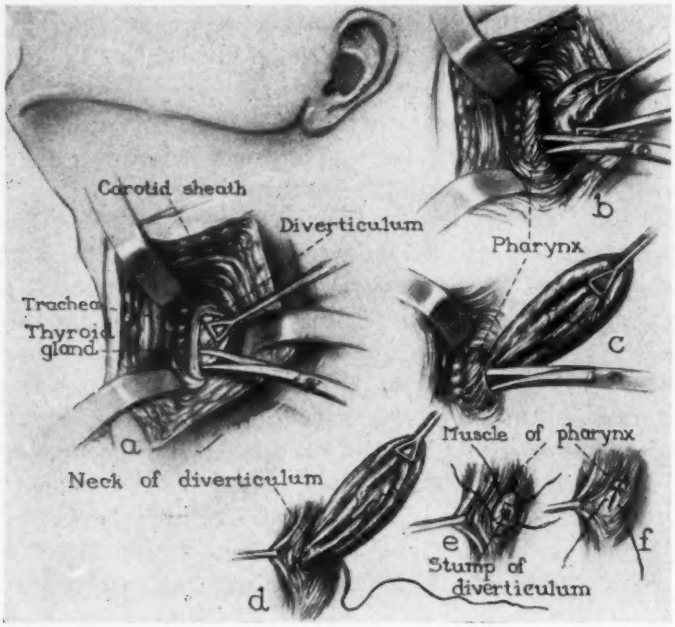

Fig. 8.—One-stage diverticulectomy. *a*, Incision along the anterior border of the sternocleidomastoid muscle, retracting the thyroid medially and the carotid sheath with the sternocleidomastoid muscle laterally. The peritracheal fascia is incised at the level of the cricoid cartilage, exposing the diverticulum. *b*, Dissecting the diverticulum from the peritracheal fascia and elevating it from the fascial planes, starting at the neck of the sac. *c*, Dissecting the true neck of the sac from the surrounding muscles of the posterior wall of the pharynx. *d*, Transfixing and ligating the neck of the sac with chromic catgut. *e*, Invagination of the stump of the sac into the wall of the pharynx. *f*, Closing the opening in the muscles of the posterior wall of the pharynx with chromic catgut.

rounded the neck of the sac are closed with interrupted catgut sutures. The silk thread which is through the esophagus is pulled taut by the anesthetist before the neck of the sac is ligated so that there is no danger of including it in the closure of the neck of the sac. A soft rubber tissue drain is placed in the pocket formerly occupied by the diverticulum but it is not placed at the site of closure of the pharyngeal wall. The wound is closed by the use of interrupted sutures.

Results of Operation.—In the 115 cases in which the one-stage operation was performed, there were no operative deaths. A temporary pharyngeal fistula developed in five cases. In three cases hoarseness occurred two to three days after operation and subsided within one week to ten days. In one case in which

the patient had hoarseness of the voice before operation, paralysis of the cord occurred and the hoarseness continued. The average duration of convalescence in the hospital was less than two weeks and the average period of time to dismissal was three weeks.

In five cases angulation of the esophagus required dilatation. The diverticula recurred in two cases. In one of these the symptoms improved after dilatation but operation subsequently may be required. In the other case, a second operation was necessary (Figs. 9, 10, 11, and 12). In this case, the diverticulum was infected at the time of the patient's first admission and had produced marked granular pharyngitis and swelling of the mucous membrane which closed the neck of the sac. This infection continued in spite of persistent efforts for three weeks before operation to irrigate the diverticulum and drain the in-

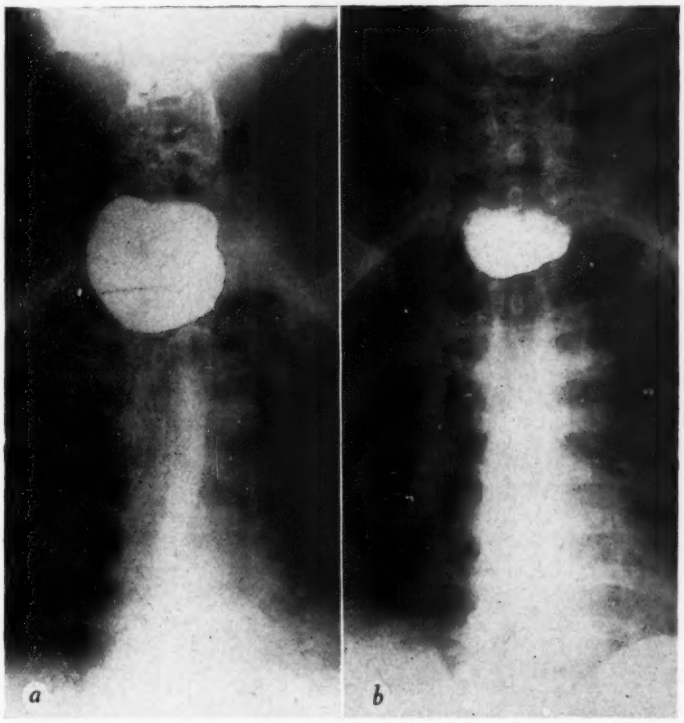

Fig. 9.—*a*, On admission, showing infected pharyngo-esophageal diverticulum extending into the mediastinum, containing several ounces of pus and producing acute pharyngitis. *b*, Four days later, showing residual barium in diverticulum, although patient has had repeated irrigations.

fection. The persistent infection presented a surgical problem; this is the only recent case in which I have considered a two-stage operation. However, a one-stage procedure was performed. Convalescence was satisfactory for ten days. Then a pharyngeal fistula developed and persisted for three weeks. Mediastinitis did not develop and the wound was entirely healed in four weeks. Subsequently a recurrence on the right side of the pharynx, which I believe was caused by weakening of the wall of the pharynx by the infection, occurred. The recurrence was noted on the roentgenogram as somewhat diffuse bulging of the right posterolateral wall of the pharynx. There was no dysphagia, but after a period of three years the patient began to have a gurgling noise and food occasionally stuck in his throat. The saceulation had progressively increased in size and operation was performed through a right cervical approach. The wound was completely healed at the time of dismissal nineteen days after operation.

This case is very instructive from the standpoint of the danger of mediastinitis associated with the one-stage operative procedure when the diverticulum is acutely infected. A pharyngeal fistula developed but there was no extension of infection into the surrounding mediastinal structures. The other four cases in which a temporary pharyngeal fistula occurred showed no signs of medias-

Fig. 10.—Diverticulum after its removal by left one-stage diverticulectomy, showing marked infection with thickening of the walls.

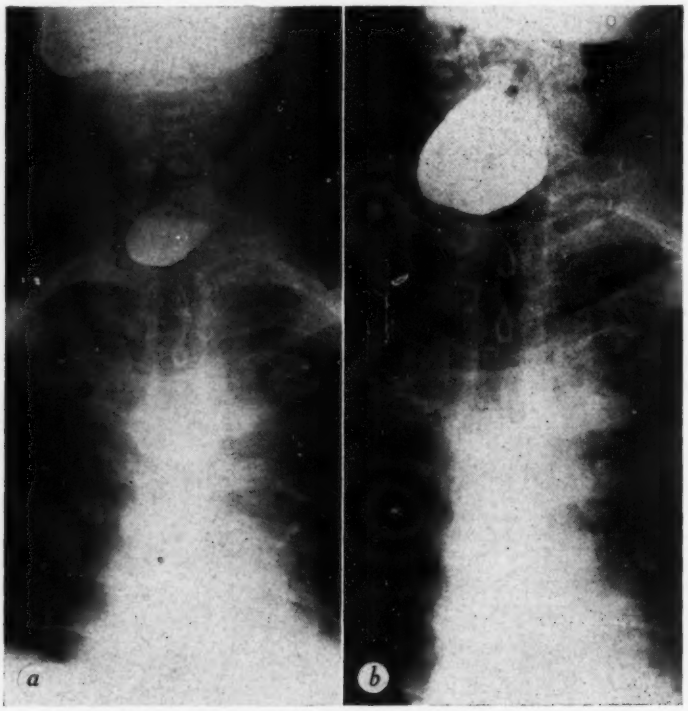

Fig. 11.—Same patient as in Fig. 9. *a*, Ten months after one-stage diverticulectomy through left cervical approach, showing moderate-sized recurrence in right posterolateral pharyngeal wall; no dysphagia. *b*, Three years after diverticulectomy, showing marked increase of the size of the recurring diverticulum in the right posterolateral wall of the pharynx; moderate regurgitation. Patient was treated by dilatations during interval.

tinitis. The earliest that a fistula developed was on the third postoperative day. This patient obtained considerable water the first night after operation without the knowledge of the nurse. Mediastinal infection did not occur, and the fistula healed within a week. The other three fistulas did not develop until after the sixth day and all closed within a week.

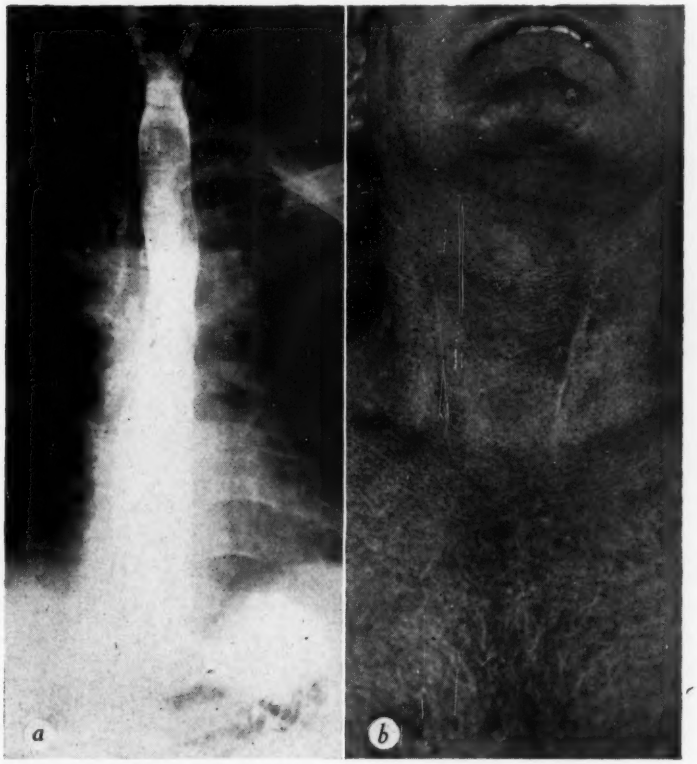

Fig. 12, *a* and *b*.—Same patient as in Figs. 9 and 11. Six months after right one-stage diverticulectomy for recurring diverticulum; esophagus normal. Both left and right cervical incisions healed, no symptoms.

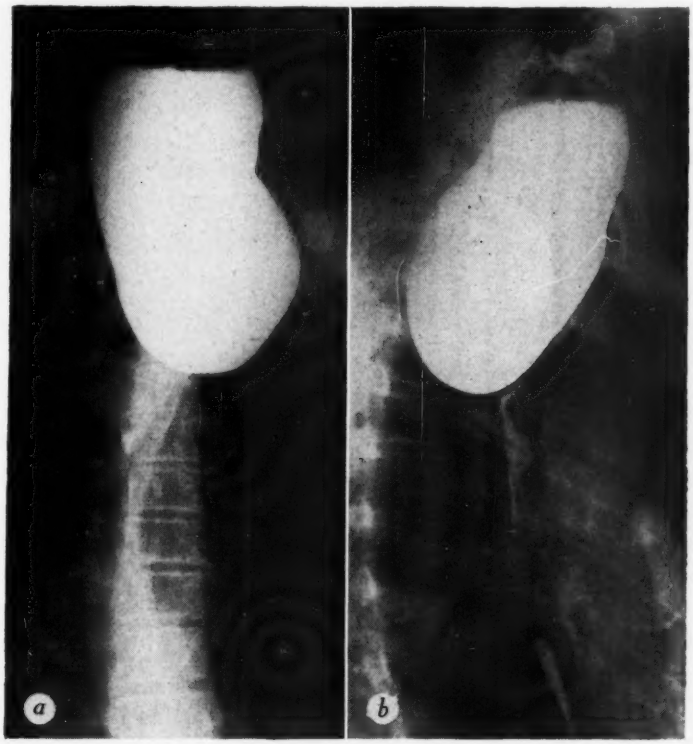

Fig. 13, *a* and *b*.—Large pharyngo-esophageal diverticulum (which held 825 c.c. of fluid) beneath the inferior constrictor and cricopharyngeus muscles. Median posterior type of diverticulum causing marked obstruction, filling the entire mediastinum and extending into the right side of the thoracic cavity.

I believe there is little risk of mediastinitis occurring after a one-stage operative procedure because in none of my cases has a fistula developed before seventy-two hours after operation. By that time the mediastinal fascial planes are walled off. However, it is important not to separate any more of the tissues of the mediastinal fascial planes than is essential and to remove the diverticulum starting at the neck of the sac.

Fifteen of the 115 patients in this series had large diverticula that filled the entire mediastinum. In several instances they extended into the thoracic cavity. As mentioned previously, the largest one held 825 c.c. of fluid (Figs. 13 and 14). There was no suggestion of mediastinal infection after operation in any of these cases.

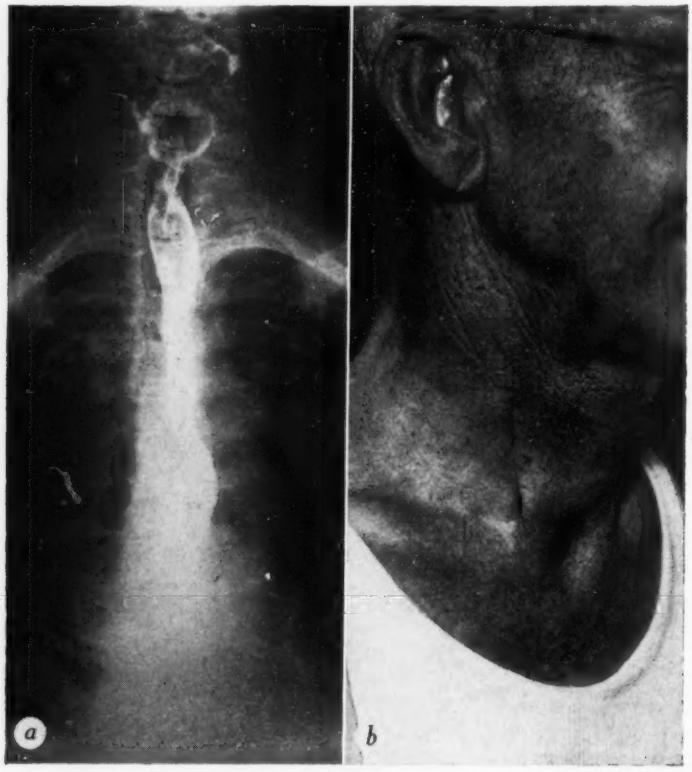

Fig. 14, *a* and *b*.—Nineteen days after one-stage diverticulectomy; right cervical approach. Esophagus normal except for slight angulation. No symptoms; incision healed.

The results of operation in the twenty-five cases in which a two-stage operation was performed are essentially the same as those reported in 1937 with the exception that one more recurrence has developed. A summary of these twenty-five two-stage operations follows: There was one operative death in the case of a patient who had Parkinson's disease. Although this death was attributed to the operation, it was the result of his poor general condition; the latter was caused by weight loss as a result of his inability to take nourishment because of the diverticulum as well as advanced Parkinson's disease. A temporary fistula developed in six cases. In three cases there was temporary hoarseness and in one case there was paralysis of one vocal cord. The average convalescence before dismissal from the hospital was more than five weeks.

Five patients had angulations that required subsequent dilatations. There were three recurrences, all of which were treated by dilatation. Two patients subsequently may require surgery.

A comparison of the results of the one-stage and the two-stage operations is shown in Table I, and a summary of the clinical data of the entire series of 140 cases as described in the text is shown in Table II.

TABLE I. DIVERTICULECTOMY FOR PHARYNGO-ESOPHAGEAL DIVERTICULUM: 140 CASES
RESULTS OF ONE-STAGE AND TWO-STAGE OPERATIONS

	ONE-STAGE*	TWO-STAGE†
Operative mortality	0	1
Temporary fistula	5	6
Temporary hoarseness	3	3
Paralysis of one vocal cord	1	1
Average convalescence	3 weeks	5+ weeks
Angulation of esophagus that required dilatations	5	5
Recurrences	2	3
Symptoms relieved by dilatations	1	3
Symptoms requiring second operation	1	0

*One-stage operation, 115 cases; marked esophageal obstruction, 15; preliminary gastrostomy, 1.

†Two-stage operation, 25 cases; complete obstruction, 3; indwelling stomach tube, 14.

TABLE II. CLINICAL DATA

Males: 107			Females: 33			Total patients: 140
Average age: 57 years			Youngest: 34 years		Oldest: 80 years	
Year:	34-39;	40-49;	50-59;	60-69;	70-79;	80
Patients:	7	25	57	38	11	2

Duration of symptoms, 1 to 25 years Average duration, 5 years
Multiple diverticula of pharynx, 1 (left side larger than right)
Occurrence in other member of family, 2
Associated conditions:
Bronchiectasis, 4; bronchitis, 9; goiter, 10; hiatal hernia, 3; esophageal diverticulum, 1; hoarseness, 8; fixed vocal cord, 2

COMMENT

Many factors, such as the condition of the patient and the type of lesion, must be taken into consideration in comparing different types of operative treatment for a surgical condition. These factors being equal, the chief consideration in determining the relative value of different procedures is the operative mortality, its effectiveness in relieving the condition, and the associated morbidity. The results obtained in these two types of operations in this series of 140 cases of pharyngo-esophageal diverticula, I believe, definitely show the value of the one-stage procedure.

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CLOSURE OF THE BRONCHIAL STUMP FOLLOWING LOBECTOMY OR PNEUMONECTOMY

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ANY method of bronchial closure, if it is to be successful, must be based upon the fundamental principles of healing. It is self-evident that there should be the least possible trauma such as crushing of tissue; that there should be accurate approximation of the surfaces which are expected to heal together; and that there should be an adequate blood supply to the tissues involved. Rienhoff and his collaborators* in an excellent article concerning the closure of the bronchus stress these matters and point out that the healing of the bronchus takes place at the cut end of its stump. Granting this premise, it is illogical to use mattress sutures which approximate the mucosal surfaces behind the cut end of the bronchus. No healing can be expected at that level and such sutures are likely to impair the blood supply by pinching off some of the branches of the bronchial artery. Rienhoff and co-workers also emphasize the importance of covering the closed bronchial stump with pleura. On the basis of these fundamental principles, the method which is most likely to succeed should:

1. Produce the least possible trauma at the end of the bronchus
2. Preserve an adequate blood supply all the way to the cut end of the bronchus
3. Approximate only the edges of the cut end of the bronchus
4. Provide adequate reinforcement of the bronchial closure by utilization of a layer of pleura sutured over the closed stump.

The method I have used is as follows. After the lobe (or lung) which is to be removed has been mobilized and the pulmonary vessels which supply it have been tied and divided separately, a large curved clamp such as might be used on the kidney pedicle is applied distal to the level which has been selected for the division of the bronchus. The purpose of this clamp is merely to prevent spilling of pus or secretions from the diseased portion of the lung and also to provide a handle with which to steady the bronchus while it is being cut across (Fig. 1, *A*). A suture of medium weight silk is then passed through the bronchial wall, tied, and held as a stay. Using a knife which is curved on the flat surface and sharpened on both edges (such as the Beaver blade No. 14), the division of the bronchus proximal to the clamp is started. One or two more silk sutures are then placed over the cut end of the bronchus and the division is completed with the knife. Several more sutures are then placed and all are tied over the end of the bronchial stump so as to approximate its cut edges. While the bronchus is being cut across, the sutures are held tightly by the assistant so as to minimize the escape of anesthetic gases. After all of the sutures have been tied, the stump is inspected for air leakage and one or more sutures are placed as needed.

Received for publication, Feb. 20, 1945.

*Rienhoff, W. F., Gannon, J., Jr., and Sherman, I.: Closure of the Bronchus following Total Pneumonectomy, Ann. Surg. **116**: 481-531, 1942.

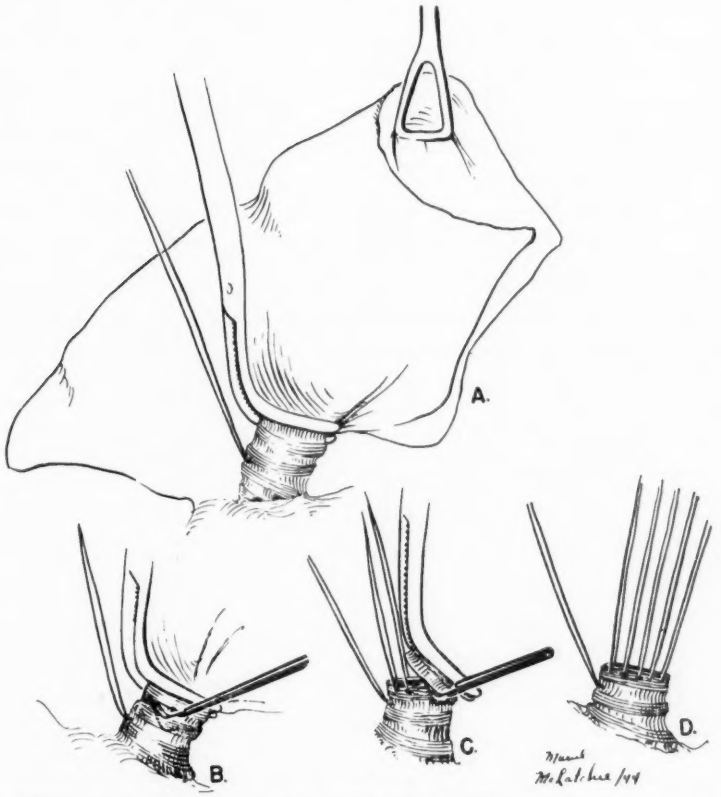

Fig. 1.—Steps in the closure of the bronchial stump. *A*, Traction suture applied. *B*, Division of the bronchus begun, using curved knife; note that the bronchus is cut across proximal to the clamp. *C*, Bronchus partly severed with two sutures applied. *D*, Division of the bronchus completed with all sutures placed.

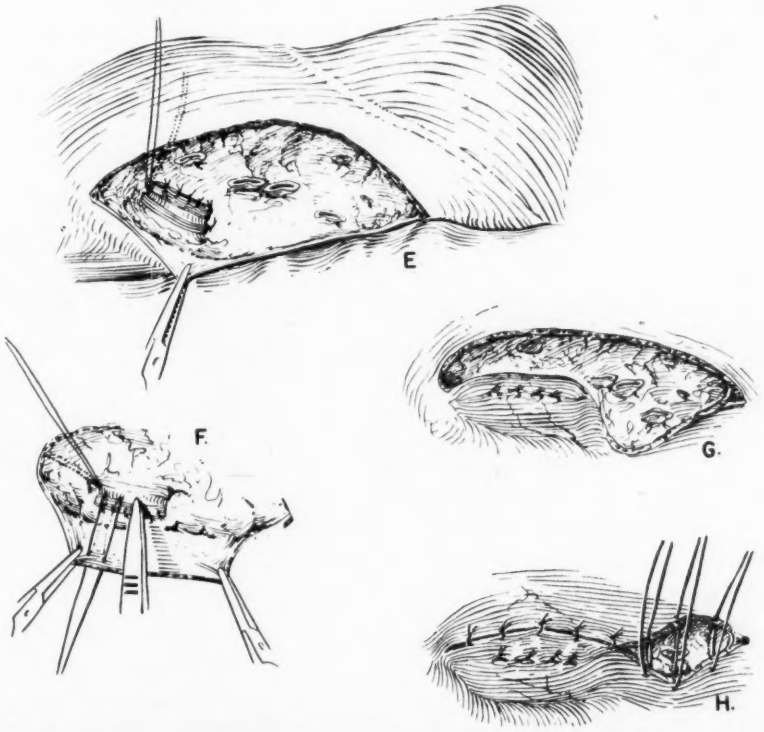

Fig. 2.—Steps in the covering of the bronchial stump. *E*, Stump after tying all sutures; flap of pleura to be sutured over held in a hemostat. *F*, First suture placed between pleural flap and side of the bronchial stump. *G*, All sutures tied, thus covering the end of the stump. *H*, Additional reinforcement possible in some cases.

There remains the important step of burying the bronchial stump beneath a flap or fold of pleura (Fig. 2). An edge of the mediastinal pleural surface, usually posterior to the region of the hilum of the lung, is almost always available. This edge is pulled over the end of the bronchial stump and fastened to the bronchus proximal to its end by means of several fine silk sutures (Fig. 2, *F* and *G*). If the pleural flap cannot be pulled over the stump easily, the tension can be relaxed by making a linear incision in the pleura several centimeters back from its edge. In many cases it is possible to add reinforcement by overlapping the opposing pleural edge as shown in Fig. 2, *H*.

This method of bronchial closure has been used in approximately 140 cases of lobectomy or pneumonectomy in the past two years. Table I shows the number and types of cases.

TABLE I. TYPES OF CASES IN WHICH THIS METHOD OF BRONCHIAL CLOSURE HAS BEEN USED

DISEASE	OPERATION		TOTAL
	LOBECTOMY	PNEUMONECTOMY	
Bronchiectasis	34	5	39
Lung abscess	22	3	25
Chronic pneumonitis	3	0	3
Tuberculosis	16	27	43
Bronchogenic cyst	1	1	2
Carcinoma	2	22	24
Metastatic carcinoma	2	0	2
Neurofibroma	0	1	1
Fibrosarcoma	0	2	2
Total	80	61	141

Leakage resulting from breaking open of the bronchial stump was known to have occurred in only one of these cases. This was a case of pneumonectomy for tuberculosis in which the primary bronchus was so embedded in calcified and caseous lymph nodes, which produced a stenosis of the bronchus, that a satisfactory closure could not be obtained, chiefly because of the necessity for cutting across diseased tissues in the bronchial wall. This man died as a result of an empyema, and at autopsy the failure of the bronchial closure was discovered. In the majority of all other instances where patients died in the hospital after operation, autopsies were performed and in no case was there any evidence of leakage from the bronchial stump. The postoperative period in these cases varied from a few days to more than two weeks.

As a result, therefore, of a considerable experience with its use, the method of closure of the bronchial stump herein described is proposed as a satisfactory technique for use in the operation of lobectomy or pneumonectomy.

LIGATION OF THE INFERIOR VENA CAVA*

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OCCLUSION of the renal veins from some progression of a thrombus in the inferior vena cava is usually fatal, although occasional reports to the contrary have appeared infrequently in medical literature.[1, 2] That pulmonary embolism from such a thrombus may be fatal is well authenticated.

One of us (R. W. B.), with collaborators,[3] has reported the utilization of femoral vein ligation in the treatment of chronic deep thrombophlebitis of the lower extremities, and at the time of that report had had occasion to ligate the inferior vena cava, subsequent to femoral vein ligation. This paper is a summary of our experiences to date in ligation of the inferior vena cava for both chronic thrombophlebitis and phlebothrombosis.

Certainly ligation of the inferior vena cava is no longer a novel procedure. The first recorded case of total ligation of the inferior vena cava was reported by Kocher in 1883.[4] The ligation was done accidentally and unknowingly during the process of dissection of metastatic carcinomatous retroperitoneal lymph nodes. At necropsy a ligature was found about the inferior vena cava. The second recorded case was reported by Billroth in 1885.[4] The vena cava was mistaken for a distended renal vein and was ligated. The patient died within one hour. The third recorded case of total ligation is that by Bottini,[5] reported in 1893. This is the first case of successful ligation, the patient making a complete recovery without circulatory complications. Since this time, a large number of reported cases has been added to the literature and Krotski,[6] in 1937, was able to collect forty-eight cases of total ligation of the inferior vena cava carried out by twenty-seven operators. Undoubtedly there have been many more caval ligations done since this report.

The earliest cases,[7] and by far the majority, were those in which accidental injury of the vena cava necessitated complete ligation of this vessel. Most of these injuries occurred during operations upon the kidney. The second largest group of cases were those in which the ligation was done during the treatment of puerperal pyemia.[8] The earliest caval ligations in this second group were three done by Trendelenburg,[8, 9] two in 1906 and a third in 1910. The first two patients died shortly after operation, while the third recovered. In more recent years, our attention has been focused upon the quiet thromboses occurring in the lower extremities, and removal of the thrombus followed by ligation of the major venous trunk has been the procedure of choice in most instances. Where bilateral involvement has occurred and rapid progression of the thrombotic process is present, ligation of the common femoral vein preceded by aspiration of the thrombus may be insufficient and ligation at a higher level may be deemed necessary. Where the involvement is bilateral, ligation of the inferior vena cava is often preferable to bilateral ligation of the external or common iliac veins. The high mortality rate formerly associated with this procedure resulted from the disease process already present or the subsequent postoperative complications, rather than from the consequences of the actual vein ligation itself.

This paper was to have been presented at the meeting of the Society of University Surgeons, New York, N. Y., Feb. 8, 1945. (Meeting canceled.)

Successful ligation of a major venous trunk necessarily implies that an adequate alternative venous route is available. The necessary anastomoses about a point of obstruction in the inferior vena cava below the level of the renal veins must, in large measure, reflect the connections involved in its embryonic development. The systemic venous drainage in very young embryos is first represented by paired longitudinal channels known as the cardinal veins.[10] The anterior cardinal veins drain the blood toward the heart from the cephalic portion of the body. In the posterior cardinal veins the blood flows forward from the caudal portion of the body. At the level of the heart the anterior and posterior cardinals on each side of the body become confluent with each other as the common cardinal veins or ducts of Cuvier (Fig. 1, *A* and *B*). The common cardinal vein from each side of the body turns mesiad and enters the sinus venosus of the developing heart. Throughout their course the posterior cardinal veins receive lateral somatic and visceral branches in more or less perfect segmental succession.

In the early stages of development, the only portion of the definitive inferior vena cava which exists is the portion which intervenes between the liver and the sinus venosus. This portion is represented by the terminal part of the right omphalomesenteric vein. The more caudal portion of the inferior vena cava is contributed to by a number of different vessels. Among these is a pair of veins developing in the ventromedial portion of the mesonephroi which is utilized in the formation of the inferior vena cava at what will be the future renal level. These are the subcardinal veins (Fig. 1, *A* and *C*). As development progresses the two subcardinals become united with one another across the midline. This union constitutes the intersubcardinal anastomosis (Fig. 1, *B* and *D*). Cephalic to the anastomosis, the right subcardinal extends forward in the mesonephros, approaching in its course a fold of the dorsal mesentery known as the caval plica. Small venous channels in the caval plica form a connection with the right subcardinal, and coursing forward empty into the developing plexus of veins in the liver. Rapid enlargement of this new small vessel in the caval plica gives rise to what is commonly known as the mesenteric portion of the inferior vena cava. Excavation of the liver sinusoids to form a main channel through the liver substance gives rise to the hepatic portion of the vena cava.

Caudal to the intersubcardinal anastomosis the inferior vena cava is derived from the right supracardinal vein. The supracardinal veins appear late in development as paired channels draining the dorsal body wall. They soon acquire anastomotic connections with the sinus as did the postcardinals earlier. Cephalic to the sinus, parts of the supracardinals persist as the azygous vessels draining in a somewhat variable manner into the reduced proximal part of the right postcardinal (Fig. 1, *E* and *F*). Caudal to the anastomosis of the supracardinals with the subcardinal sinus, they gradually become the principal drainage channels of blood returning from the legs and pelvis. With the anastomosis of the right and left iliacs (old postcardinal tributaries), the blood returns increasingly by the right supracardinal which gradually enlarges to form the postrenal portion of the inferior vena cava. Vestiges of the left supracardinal vein are represented by longitudinal channels known in the adult as the ascending lumbars (Fig. 5), which become continuous with the azygous system superiorly and in this manner are associated directly with the superior vena caval system (Fig. 1, *E* and *F*). Likewise, small accessory supra-

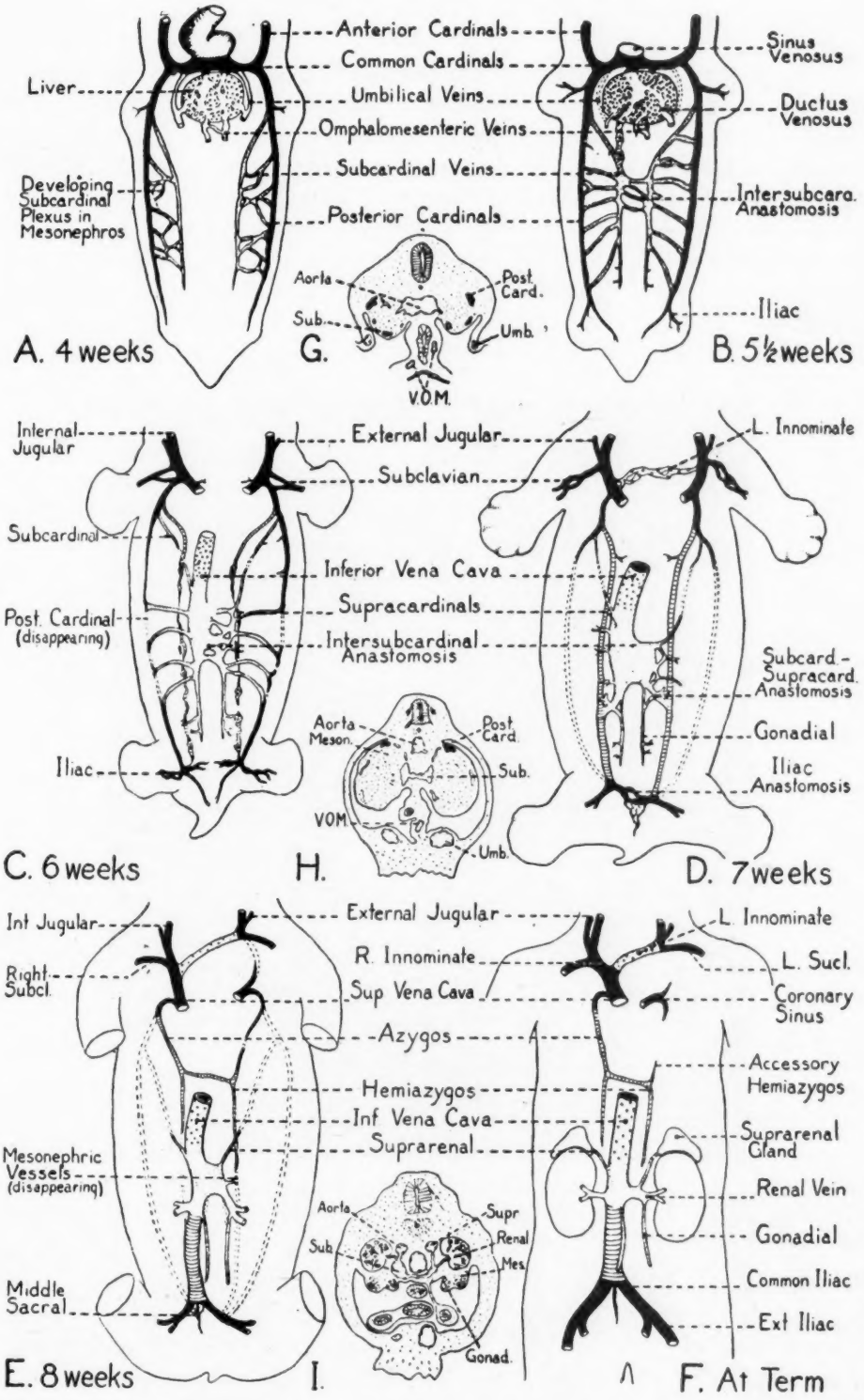

Fig. 1.—Schematic ventral views showing some of the steps in the development of the inferior vena cava. The cardinal and omphalomesenteric veins are shown in black, the subcardinal system is stippled, the supracardinals are horizontally hatched, and vessels arising independently of these three systems are indicated by small crosses. (Diagrams by Patten, based on the work of McClure and Butler, from Morris' Human Anatomy, Philadelphia, The Blakiston Company.)

cardinal channels on the right represent vestiges of the primitive condition when, as is the case with all developing main channels, the vessels in that location were plexiform.

This plexiform arrangement retains its embryonic configuration about the vertebral column in the form of the intra- and perivertebral plexus of veins (Fig. 6). These vessels lack the longitudinal arrangement of the more highly developed channels, possibly because during embryologic life the return flow of blood was cared for primarily by the developing inferior vena cava. These primitive vessels communicate with the inferior vena cava through segmental branches and play an important role in the passage of blood about a point of ligation of the inferior vena cava. They communicate with the ascending lumbars and azygous system and thereby maintain communications with the inferior and superior vena cava throughout the length of the spinal column.

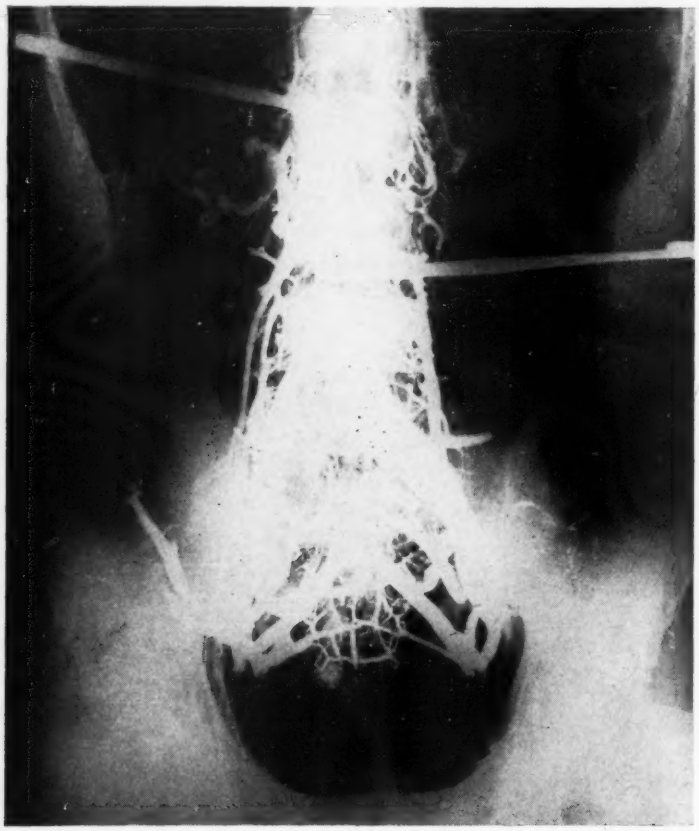

Fig. 2.—Roentgenogram of the injected veins of the pelvis of a cadaver following clamping of the inferior vena cava with hemostats at two levels below the entrance of the renals. The extensive filling of the pelvic and vertebral vessels, as well as the ascending lumbars and section of inferior vena cava between hemostats is well shown.

Although we have been aware of the fact that caval ligation in cases of acute ascending thrombophlebitis and phlebothrombosis involving the pelvic vessels is a life-saving measure, we have been reticent to employ this procedure because of the widespread importance placed upon the continuity of this largest vein of the body. With this in mind, one of us (R. O. N.) with an associate[11] attempted to determine the more important pathways by which blood is returned to the heart following ligation of the inferior vena cava below the renal vein. Unimbalmed cadavers were eviscerated and the aorta and its branches removed to facilitate work with the veins. The superior vena cava was ligated at its entrance into the heart and the inferior vena cava was

removed from the region of the renal vein superiorly. A No. 10 cannula was inserted into the femoral vein by way of the saphenous on one side and the system irrigated with warm saline to extricate as much clotted blood as possible. When a free flow of saline solution was obtained, the inferior vena cava was clamped just above the bifurcation and again in the region just below the renals. Warm saline solution was again allowed to flow through the system, this time in an attempt to cleanse the collateral system. A thin suspension of red lead was forced into the system under ten pounds of pressure for a period of one minute, following which the cannula was removed and the saphenous vein ligated. Roentgenograms were taken and the injected venous channels dissected.

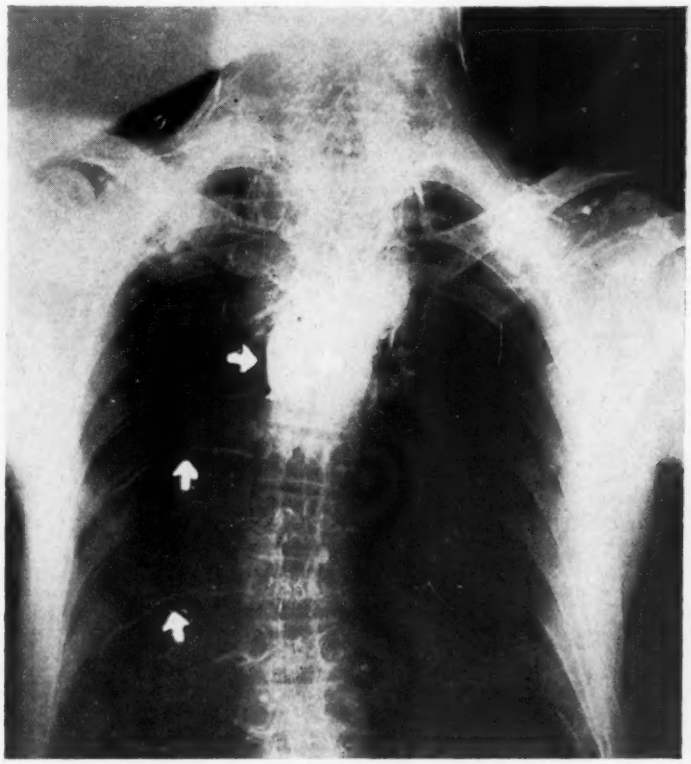

Fig. 3.—Roentgenogram of the thorax of an injected cadaver showing the extensive filling of the intercostal and vertebral vessels as well as the superior vena cava. The injection was by way of the femoral vein and followed ligation of the inferior vena cava below the renal level and excision of the inferior vena cava above the level of the renals.

In no case, during the period of lead injection, was there delay in filling of the inferior vena cava above the lower clamp (Fig. 2). The superior vena cava rapidly filled (Fig. 3), as might be anticipated, by way of the ascending lumbars and the segmentals which associate directly with the vertebral plexuses through the spinal veins and above the diaphragm by the azygous system which receives the segmental veins and terminates in the superior vena cava. Communications between the inferior vena cava and the vertebral systems are as follows: (1) Four segmental tributaries of the lateral sacral veins pass medially from the hypogastric veins to enter each of the anterior sacral foramina to communicate with the internal vertebral plexus (Fig. 4). (2) Two large ascending lumbar veins on each side pass from the common iliac veins upward along the lateral aspect of the vertebral bodies (Fig. 5). These anastomose with one another and become continuous superiorly with the azygous

system. At each segment these veins communicate with the external and internal vertebral plexuses by way of the segmental spinal veins passing through the intervertebral foramina, and with the anterior vertebral veins contributing to the external plexus. The external plexus also anastomoses with the basivertebrals through the vertebral bodies, which are themselves tributaries of the internal plexus (Fig. 6). An inconstant middle sacral vein passes from the common iliac downward over the sacrum, anastomoses with the lateral sacral veins, and passes directly into the vertebral plexus through the sacrococcygeal foramina. (3) Laminectomy revealed the large internal vertebral plexus on the surface of the dura mater of the spinal cord (Fig. 6). It also showed the large venous sinuses running more or less longitudinally on each side, ventrolateral to the dura. These veins were all very well filled with the injected media. (4) The intra- and perivertebral plexuses communicate with the segmental veins which in turn drain into the vena cava.

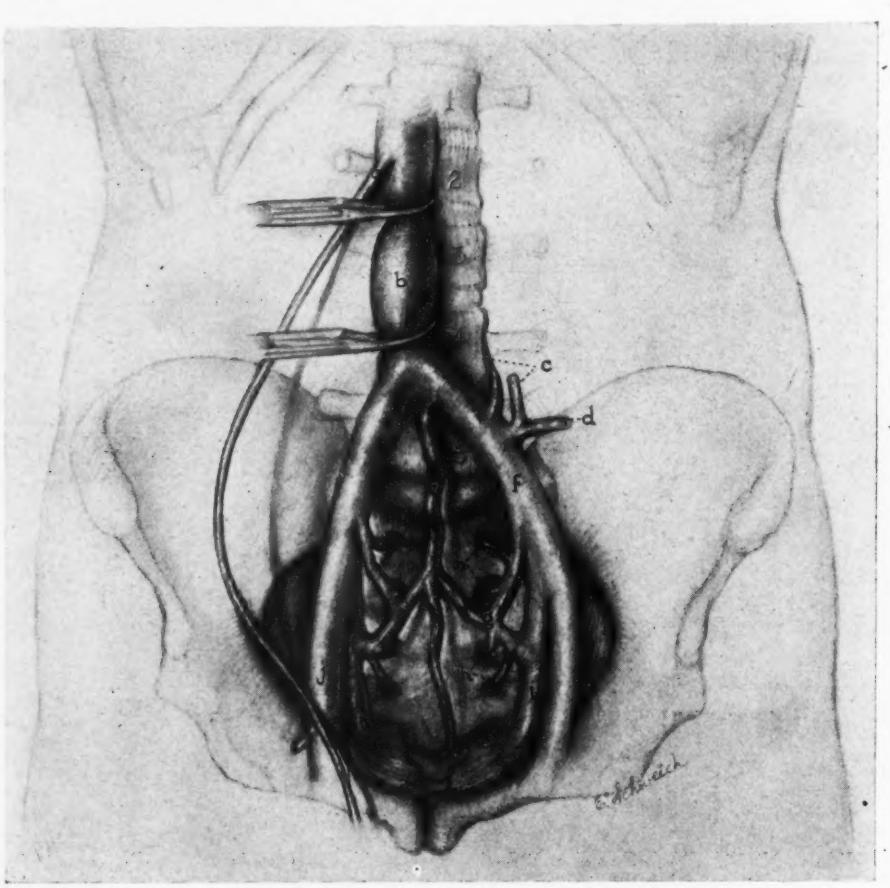

Fig. 4.—Drawing made from an injected cadaver to show the plan of the veins of the pelvis. The vena cava has been ligated so all anastomotic vessels below the obstruction appear strongly dilated.

By means of these plexuses about the vertebral column, plus the free anastomoses about the point of obstruction, there was ready filling of the vena cava above the obstruction, of the azygos system, the intercostal veins, and the superior vena cava. Since all abdominal viscera were removed, communications with the portal system were not verified.

The inferior vena cava has been our site of election of vein ligation in ten patients. In three patients saphenous ligation had been done at an earlier date. In one patient a femoral vein ligation, above the level of the profunda

femoris branch, had been done, and in another patient ligation of the right ovarian vein was carried out at the time of caval ligation. The first patient of this group was operated upon twelve months ago. The most recent caval ligation was done within one month of this writing. In no patient of this group have anticoagulants been used in either the preoperative or postoperative period.

The patients here reported were seen during various stages of the disease. One patient was seen one day following the onset of leg edema, and the onset, signs, and symptoms were characteristic of the syndrome frequently spoken of as phlebothrombosis. None of the remainder of the patients was seen at the time of onset of the thrombotic process. In seven of the patients the character of onset as well as some of the immediate sequelae indicated a bland thrombosis of the deep venous system. In two patients the onset suggested a femoro-iliac thrombosis. One patient developed a deep suppurative thrombophlebitis following the injection of a sclerosing substance for the treatment of varicose veins. Chronic thrombosis had recurred in one patient over a

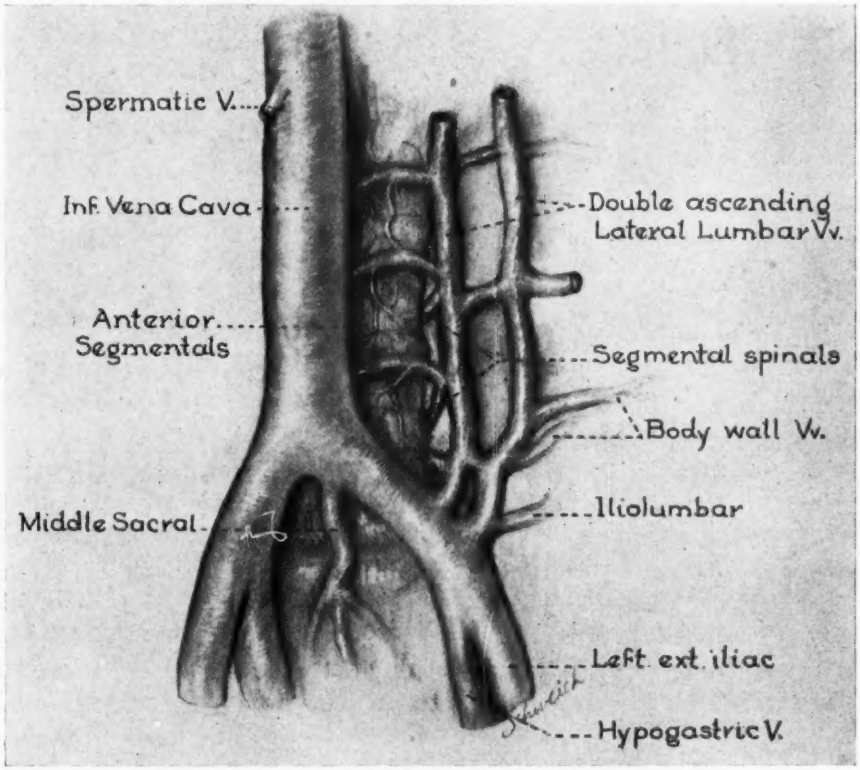

Fig. 5.—Drawing made from an injected cadaver showing the connections between the ascending lumbar veins and the vertebral plexus of veins.

period of ten years. In three patients there was a definite clinical history of one or more pulmonary infarcts; in three patients definite evidence of pulmonary infarction was present at the time of operation. One patient gave an atypical history of substernal oppression which had been diagnosed and treated as pylorospasm prior to the onset of the thrombosis. No roentgen evidence of pulmonary embolism was obtained. This last patient has been followed for a period of four months since caval ligation without recurrence of the abdominal symptoms. No thrombus was present within the cava at the time of operation, so that phlebotomy and thrombectomy were not indicated. In three patients

there was no history suggesting embolism with pulmonary infarction. Five of the ten patients had had chronic recurring ulcerations of the lower extremities prior to caval ligation. In one patient, whose symptoms had been present for a period of eight months, low back pain was a predominant symptom. In two other patients low back pain has been present for a variable period postoperatively. In three patients distention of the superficial lower abdominal veins has been remarkable. The patients in this series vary in ages from 27 to 74 years. Thus, of the ten patients, three presented themselves because of multiple, recent pulmonary emboli (one of these had also chronic recurring leg edema with ulceration), four because of chronic edema of the legs with ulceration, two because of painfully swollen legs without ulceration, and one because of epigastric pain associated with phlebothrombosis.

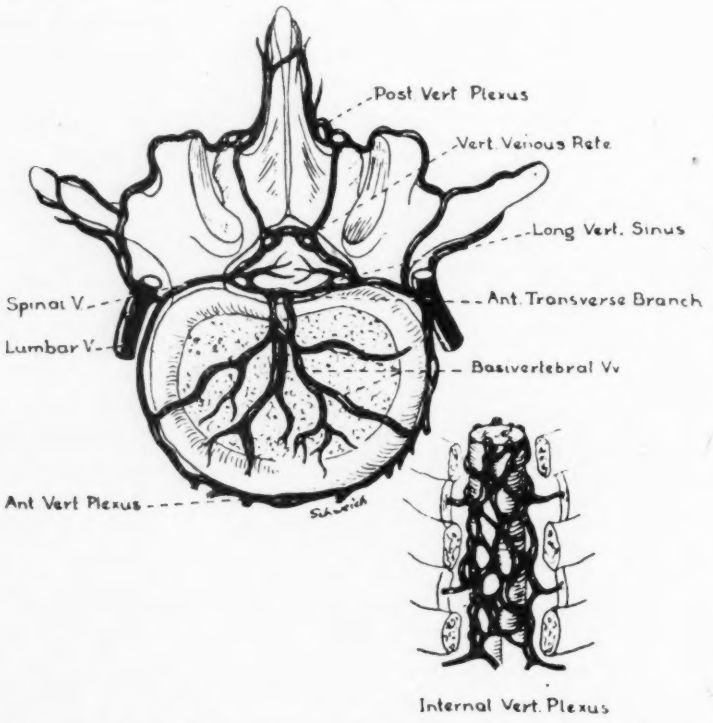

Fig. 6.—Diagrammatic sketch of the inter- and perivertebral plexus of veins. (From Morris Human Anatomy, Ed. 10, Philadelphia, 1942, the Blakiston Company.)

In each instance the inferior vena cava was exposed just above its bifurcation through a right transverse incision made at the level of the umbilicus and in each instance the entire exposure was retroperitoneal. In one patient, not considered in this series, an unsuccessful attempt was made to isolate the inferior vena cava but the structure could not be identified. There was considerable enlargement on the retroperitoneal lymph nodes with much perinodal reaction about these structures, and a subsequent diagnosis of lymphoblastoma was verified. Various types of ligature material have been used including No. 1 black silk, No. 1 chromicized catgut, and ¼ inch cotton umbilical tape. The latter material has been used with the greatest frequency. In only one instance was the vena cava transected following ligation. In the remainder of the cases, the vessel was ligated in continuity. Postoperatively, compression bandages were kept continuously about the lower extremities and the patients were encouraged to move about freely in bed. External supports were advised in all instances until no further edema was present in the legs after sustained activity.

In no patient did severe swelling occur in the immediate postoperative period. However, all patients had a varying degree of swelling immediately postoperatively and this increased to a variable degree after mobilization began.

We noted a mild flare-up of the thrombotic process in two patients during the course of their convalescence, and in a third patient this process was quite severe, involving not only the superficial but the deep venous channels. This latter patient had had a suppurative form of thrombophlebitis with a staphylococcus septicemia one year prior to caval ligation.

Ligation of the inferior vena cava is attended by a variable, but usually marked, increase in the venous pressure in the lower extremities. In two patients this necessitated numerous ligations of prominent varicose veins in the legs, and in another, ligation of the enlarged thoraco-epigastric veins. These ligations were not attended by increased swelling in the legs. The venous pressure has remained elevated to a varying degree in all patients to date. In the one patient upon whom ligation was carried out twelve months ago, the venous pressure in the legs is still twice that in the upper extremity although he is free of edema.

Since it is conceded that there is probably increased venous blood flow through the paravertebral venous plexus as a result of the numerous anastomoses conducting blood into this system, it was feared that varices might well occur in this system. There have been no clinical symptoms to suggest that varices have occurred in any patient. Measurement of the venous pressure in this system has not been undertaken. However, examination of spinal fluid pressures, and quantitative chemical analysis of the spinal fluid in patients have failed to give any indication of abnormalities which might result from an increased filtration pressure. All pressures were within the accepted normal range, and levels of total protein, chlorides, and sugar were also within normal limits. These studies were carried out on patients two weeks, five months, and twelve months following caval ligation.

The chronic supramalleolar ulcers which were present in five patients have shown a varied response to caval ligation. In one patient the ulceration healed during the immediate postoperative period and has remained healed for four months. In a second patient the ulcer healed, only to recur with the appearance of superficial surrounding varices. Healing occurred only after these were ligated and there has been no further recurrence in eight months. In a third patient similar healing and recurrence occurred. Following a period of bed rest for one week, complete healing resulted. The entire healed area has been recently excised and a graft applied. In the two remaining patients healing occurred in the immediate postoperative period but the time elapsed since operation has been too short to determine whether these ulcers will remain healed or whether further treatment will be necessary.

All patients are still wearing external supports, elastic knee-length hose or elastic bandages. By this means the edema of the legs is well controlled. In the one patient upon whom caval ligation was done twelve months ago, these have been removed intermittently for short periods, without recurrence of edema. The venous pressure in the legs of this patient is 270 mm. H_2O, twice that in the upper extremity, and some 70 mm. above the arbitrarily accepted level at which his edema might be expected to appear.

From our experiences to date an adequate collateral circulation, as evidenced by a normal venous pressure, may not be expected in those individuals with a long-standing thrombosis of the deep venous system of the lower ex-

tremities, in less than twelve months after ligation of the inferior vena cava. However, the clinical appearance of edema is easily prevented and controlled by the use of elastic external supports. The degree of immediate postoperative edema is minimal. This is in contrast to the sometimes severe and profound swelling which occurs occasionally after femoral vein ligation. We feel that the degree of immediate postoperative edema, and probably its duration, is greatly lessened as higher levels of venous ligation are carried out. The operative procedure has been well tolerated by these patients and no fatalities have occurred.

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OSTEOMYELITIS OF THE SKULL—ITS TREATMENT WITH PENICILLIN AND REPAIR OF THE DEFECT WITH TANTALUM

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OSTEOMYELITIS of the frontal bone, secondary to frontal sinusitis, is one of the most fatal of surgical diseases. Its treatment is often unsatisfactory because spread of the infection is difficult to control by the ordinary methods, particularly in the acute fulminating cases. The primary infection, acute sinusitis, is fairly common, but the complication of frontal osteomyelitis is relatively uncommon. Accurate statistics on the incidence of frontal osteomyelitis secondary to frontal sinusitis are not available. Certainly more cases occur than the number published in the literature. Yerger[15] reported 125 cases collected from the literature up to 1931, but gave no estimate as to the percentage incidence. In a series of eighty-six cases of frontal sinusitis reviewed by Mac Millan,[10] thirty-six (40 per cent) showed extension to frontal osteomyelitis, with a mortality of 14 per cent. This incidence of 40 per cent osteomyelitis is certainly much too high in an over-all review of frontal sinusitis. In cases of frontal osteomyelitis, Ballinger and Ballinger[1] gave an over-all mortality of 35 to 79 per cent and feels that it is much higher in the postoperative than in the spontaneous cases.

Received for publication, Dec. 13, 1944.

The anterior and posterior walls of the frontal sinus correspond to the outer and inner tables of the skull respectively, so that extension of infection within the sinus up into the diploic spaces of the frontal bones is an obvious possibility. The veins of the mucous membrane of the frontal sinuses are continuous with the diploic veins of the frontal skull. The diploic veins (Breschet veins) are nutrient vessels derived chiefly from the intracranial vessels through the inner table, so that the dura seems to attract the infection more strongly through the inner table than through the outer table periosteum.

In infections of the frontal sinus, the offending organism is usually the *Staphylococcus aureus* and occasionally hemolytic streptococcus or pneumococcus. If a thrombophlebitis supervenes in the sinus infection, the infection extends upward into the marrow between the tables of the skull where the circulation is of the closed (sinusoidal) type. The organisms extend by contiguity or in some instances by embolism, so that diffuse spreading or local islands of osteomyelitis occur. McCollum[12] states that the presence of bacteria leads to necrosis of surrounding tissue and the fact that this necrosis extends for a wider area than the clumps of bacteria means that they produce a toxic substance. These changes have been adequately described by Mosher[13] and Furstenberg.[5]

It is well known that osteomyelitis is usually a slow disease, even in acute cases, and its manifestations depend on the virulence of the organism and resistance of the host. In discussing its phases, it is frequently divided into two types: (1) acute (fulminating) and (2) chronic (less virulent forms).[14] Brunner[3] subdivides the acute into (a) fulminating and (b) protracted types; and the chronic into (a) primary and (b) secondary forms. This classification, although having some clinical support, is too cumbersome for average use and is admittedly considered indefinite. Williams and Nichols[17] conveniently divide frontal osteomyelitis into three types: (1) fulminating; (2) localized, self-limiting type that heals spontaneously; and (3) the slowly spreading type that forms Pott's puffy tumor (pericranial abscess). From a review of the literature it appears that the acute form can be designated as that in which the osteomyelitic process is spreading and has associated systemic reaction of varying degree. The chronic form can be designated as the localized "burned out" type with repeated sequestrum formation and little or no systemic reaction. The three cases to be presented here can be called acute osteomyelitis, spreading, but not fulminating type. The fulminating form most commonly follows swimming, has a very rapid course, and carries a high mortality due to intracranial extension.

The diagnosis is made early by evidence of pain and extending pitting edema of the scalp, and by x-ray changes manifested by a "smudge" that is due to the loss of the discrete mucoperiosteal outline of the frontal sinus. Ten days to two weeks later, when the area of demineralization has assumed the characteristic "moth-eaten" appearance, the diagnosis is no longer in doubt.

The form of treatment varies with the exigency of the case at hand. In the fulminating type with the patient critically ill, and manifested by pitting doughy edema of the forehead, it is imperative to do wide

radical removal of the diseased osteomyelitic bone. Fred[4] advocated the use of sulfonamide drugs in addition to operation and states, "I am convinced that chemotherapy will surely modify, even revolutionize the treatment of osteomyelitis—but incision and drainage must be instituted as well." The dependency on sulfonamide drugs is challenged by Jones,[7] who feels that these drugs have their limitations in the treatment of such conditions. The bacteriostatic properties of sulfonamide therapy in staphylococcus infections are inhibited by increased synthesis of para-amino benzoic acid at the site of infection. Our experience shows that penicillin has definitely revolutionized the treatment of osteomyelitis of the skull of sinus origin in that it is an excellent bacteriostatic agent, overcomes the infection rapidly, and limits its spread, thus permitting early operation with primary closure of the wound and rapid recovery. Until recently, the classical inverted T incision was used with open packing of the wound and subsequent deforming scar of the forehead.[2, 14] With the use of penicillin, a coronal incision is preferable, giving a more adequate exposure and allowing the removal of the diseased bone in one piece, so avoiding a deforming scar of the frontal scalp. When healing is complete and all evidence of infection has disappeared, cosmetic repair of the underlying bone defect with insertion of a tantalum plate is carried out easily. The restoration of the smooth contour of the forehead is easily accomplished.

CASE REPORTS

The following three cases to be reported involved young adults in Military Service and will be given in the sequence of hospital admission. It so happens that the first patient was the most critically ill and the second and third less ill, consecutively.

CASE 1.—G. M., aged 27 years, was admitted to Bushnell General Hospital, July 4, 1943. This aviation cadet gave a history of chronic sinusitis for several years and was treated by having a submucous resection in 1938 and removal of nasal polyp October, 1942. He was in good health until his present illness except for occasional nasal obstruction and postnasal discharge. On routine physical examination, March 27, 1943, he was found to have a right pansinusitis and so was admitted to a Station Hospital for its correction. Treatment consisted of daily nasal irrigations for ten days and as there was no improvement, a right intranasal antrostomy was done April 5, 1943. His condition remained good for the first seven days postoperatively, but on April 12, 1943, he developed a slight fever, some swelling of the right side of the face and eyelid, and pain. He was treated with hot compresses, and started on sulfadiazine, 6 Gm. daily. His temperature elevation subsided for three days and then began a steady progressive daily elevation, reaching 103° F. and an extension of a fluctuant swelling into the right canine fossa. April 21, 1943, this was incised. The infection continued to spread so that between April 21 and June 4, 1943, he had seven operations carried out in the right antrum, ethmoids, both frontal sinuses, and the forehead scalp, but without improvement. By May 24, 1943, he had developed pitting edema of the left side of the forehead and on May 26, 1943, the first signs of osteomyelitis of the frontal bone were evident by x-ray. During his entire three months' treatment at a Station Hospital he had received 442 Gm. of sulfadiazine with a sustained blood level of 7.1 to 13.6 mg. per cent but without apparent benefit. He had also received 3,200 c.c. of whole blood in nine transfusions. The culture of all the abscesses showed nonhemolytic staphylococcus.

He was transferred to Bushnell General Hospital July 4, 1943, because of the spreading frontal osteomyelitis. Examination on admission showed a chronically ill, undernourished patient with multiple draining sinuses of the right side of the

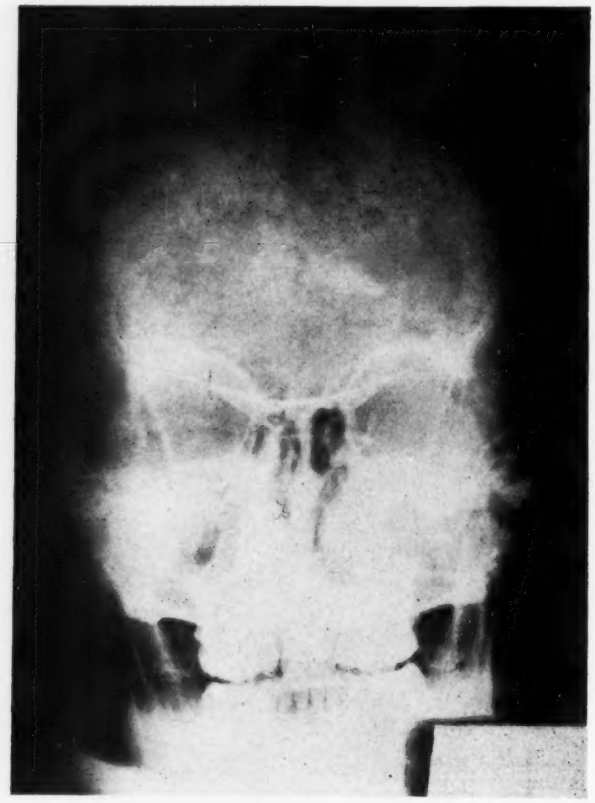
face and forehead, all exuding frank pus. He was clear mentally and cooperated well. The systemic review was negative. Complete neurologic examination was normal except for complete anosmia, proptosis and chemosis of the right eye, and a diplopia in all directions. There was anesthesia of the first and second divisions of the fifth nerve on the right side and a right facial weakness of peripheral type. The remainder of the examination was negative. Lumbar puncture showed a pressure of 150 mm. of water and the fluid contained five cells, total protein 50 mg., and the smears and cultures showed no organisms. Blood studies showed red blood count, 4,190,000, with hemoglobin, 82 per cent; white blood cells, 14,800; polymorphonuclears, 75 per cent; lymphocytes, 21 per cent and eosinophiles, 4 per cent; hematocrit, 40 per cent; sedimentation rate, 53 mm. per hour; plasma protein 7.3; blood chlorides, 585. Cultures of the draining sinuses of the face and forehead showed hemolytic *Staphylococcus aureus,* coagulase positive. The diagnosis on admission was osteomyelitis, acute, severe, right maxilla, ethmoid and frontal bones, secondary to chronic pansinusitis. There was no neurologic evidence of intracranial extension. (Figs. 1 and 2.)

Fig. 1.—G. M., Case 1. Admission photograph, taken July 5, 1943, showing multiple draining wounds prior to administration of penicillin.

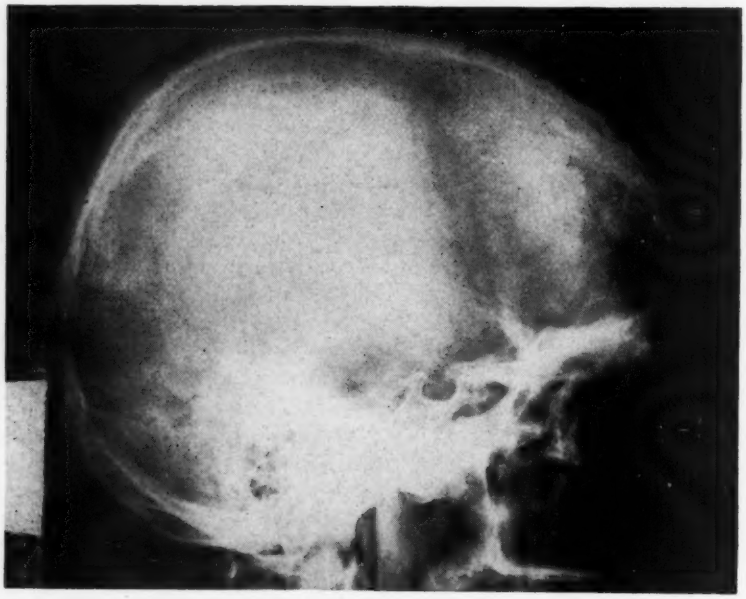
Course in Hospital.—Immediately after basic laboratory studies had been carried out, the patient was started on penicillin, being given 240,000 units intravenously daily for five days, July 5, 1943, to July 10, 1943, a total of 1,200,000 units.* Penicillin was also instilled locally into the draining sinuses (250 units per cubic centimeter). From July 10 to July 30, 1943, he was continued on 120,000 units intravenously, daily, receiving a total of 2,400,000 units during the twenty days. By July 24, 1943, all purulent discharge had stopped, temperature was normal, and he was much improved. It was thought the infection had been eradicated, but on Aug. 16, 1943, a purulent collection appeared in the forehead on the left side and was drained through a previous incision. Penicillin was again administered for another twelve days (total 2,040,000 units). The infection cleared again only to reappear in the forehead on the right side Sept. 6, 1943. It became evident that penicillin could readily control the infection but not overcome it, and some more radical measures were necessary. Penicillin was administered for the third course, a total of 360,000 units over three days. During the entire interval of treatment with penicillin, the patient received a total of 6 million units from July 5, 1943, to Sept. 10, 1943.

*The dosage used was that originally instituted by Lyons.[9]

Sept. 10, 1943, the first stage operation for frontal osteomyelitis was carried out. Through a coronal incision a transverse channel 1 cm. wide was removed along the coronal suture line behind the edge of diseased bone, and the external periosteum folded under healthy bone edge, as described by Schilling,[15] and recently Van Wagenen.[16] Penicillin was instilled locally to the forehead until



A.



B.

Fig. 2, *A* and *B*.—G. M. Preoperative x-ray views, anteroposterior (Aug. 28, 1943) and lateral (Sept. 7, 1943), showing the extent of the frontal osteomyelitic process.

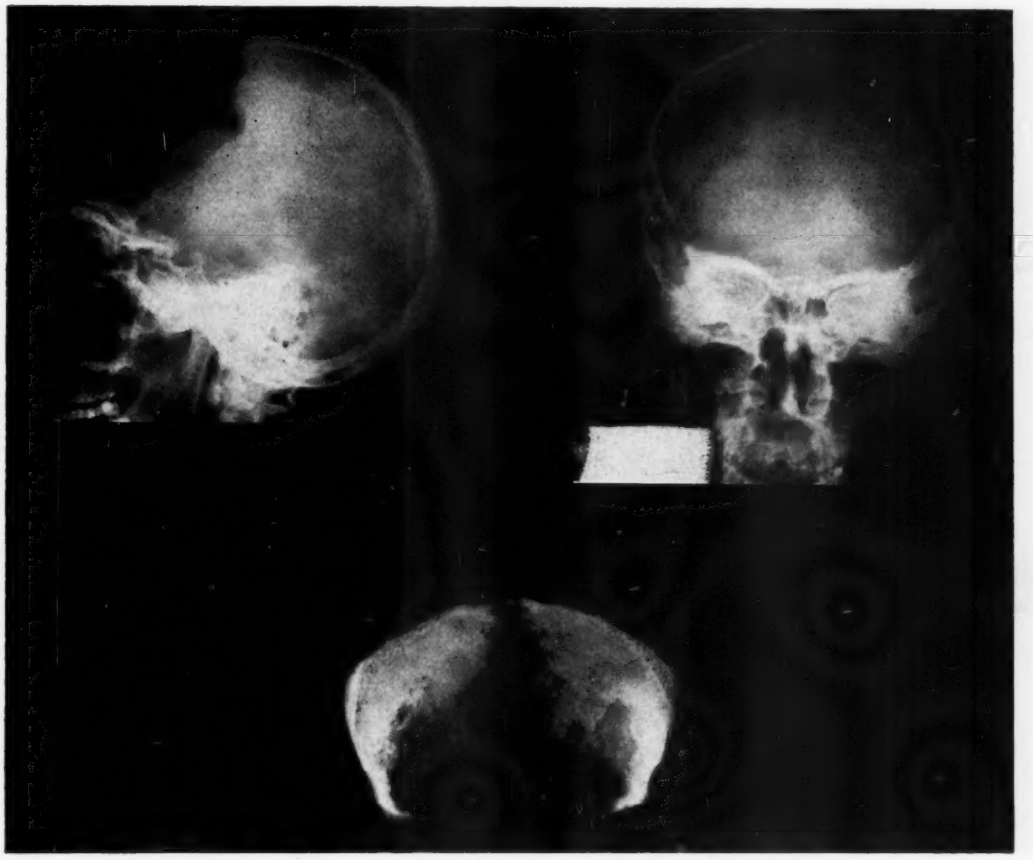


Fig. 3.—G. M. Postoperative x-ray pictures, anteroposterior and lateral, showing frontal skull defect and the excised bone fragment. (Nov. 18, 1943.)

A. *B.*

Fig. 4, *A* and *B*.—G. M. Photographs taken two weeks postoperatively, Oct. 25, 1943, showing the coronal incision, slight depression of the forehead area, and healing of all the former forehead sinuses.

Sept. 17, 1943, when through the same coronal incision the entire skull anterior to the coronal suture was removed in one piece. There was one small area of granulation tissue on the dura, but no frank pus and no perforations were noted. A complete radical frontal operation was also carried out, preserving the supraorbital ridges. The wound healed per primum in five days, during which time he was given sulfadiazine, since he had become penicillin-resistant at the time of operation.[10] (Figs. 3 and 4.)

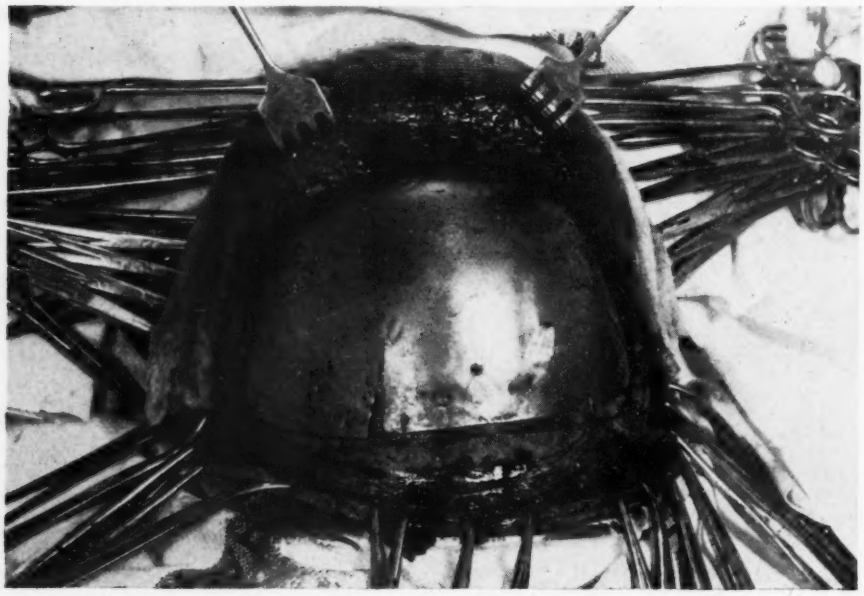
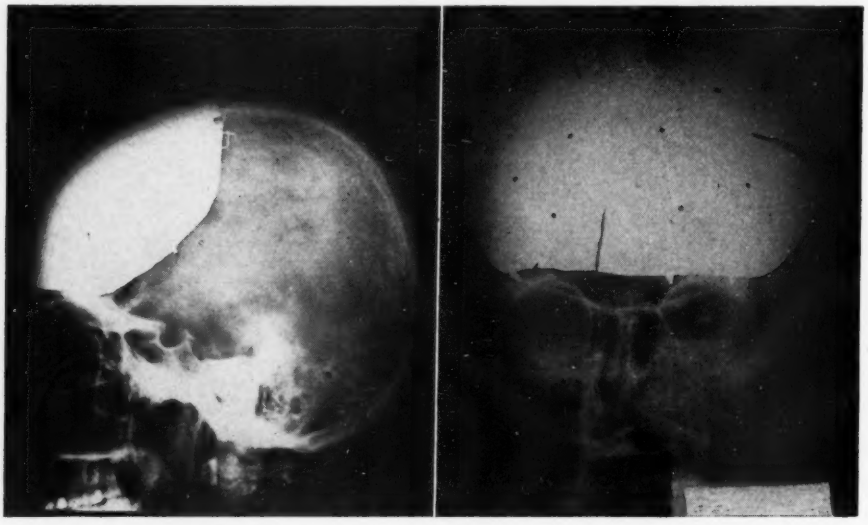


Fig. 5.—G. M. The tantalum plate anchored in position by means of tantalum wire (May 1, 1944). Note perforations referred to in text.



A. *B.*

Fig. 6, *A* and *B*.—G. M. Postoperative x-ray anteroposterior and lateral views, May 17, 1944, showing tantalum plate firmly fixed in position.

He made a rapid recovery and became a librarian in the hospital. However, because of the large frontal defect, he desired a protective covering for the forehead, and so after making a plastic mold of the defect, a large tantalum plate was formed that weighed 105 Gm. and was 250 sq. cm. in size. (See technique under Discussion.) On May 1, 1944, the entire frontal scalp was turned down easily off the underlying dura through the former incision and the tantalum plate

solidly wired into place. The cosmetic result was considered excellent by the patient. He has been returned to limited duty and plans to have plastic operations about the old drainage scars done at a later date. (Figs. 5, 6, and 7.)

Comment.—This patient harbored a spreading frontal osteomyelitis for at least six weeks while under sulfonamide drug medication, without any improvement. After receiving systemic and local penicillin, improvement was dramatic after the first week, only to be followed by a relapse shortly after penicillin was discontinued. This occurred a second time, indicating that penicillin is an excellent bacteriostatic and not a bacteriocidal agent. It also shows that surgical removal of the diseased bone is usually necessary to effect a cure.

A. *B.*

Fig. 7, *A* and *B*.—G. M. Anteroposterior and lateral photographs taken May 2, 1944, after insertion of tantalum plate to show restoration contour of frontal skull; facial scars to be corrected by plastic procedure.

CASE 2.—K. S. D., aged 37 years, was admitted to Bushnell General Hospital, Jan. 10, 1944. This soldier's past history was negative except for an auto accident in 1935, in which he sustained lacerations on the right side of the forehead, and epigastric distress since 1941.

He entered the service in September, 1943. One month later, Oct. 19, 1943, he entered a station hospital, complaining of epigastric pain of about two years' duration. A gastrointestinal x-ray made Oct. 23, 1943, showed the presence of a duodenal ulcer. At the same time he developed a severe nasopharyngitis that rapidly progressed into a pansinusitis. Treatment consisted of hot compresses, nasal shrinkage, and sulfanilamide, 1 Gm. four times a day. Oct. 30, 1943, he demonstrated furuncles of the nose with cellulitis, and an impending cavernous sinus thrombosis was suspected. At the same time he showed suppuration of the ethmoid and left maxillary sinuses. Sinus irrigations were carried out intermittently until Dec. 8, 1943, when a left frontal sinusotomy was done, but culture of the pus showed no growth. Blood count showed red blood cells, 4,870,000, with hemoglobin, 95 per cent. White blood count was 11,550; polymorphonuclears, 75 per cent; and lymphocytes, 25 per cent. Dec. 14, 1943, a similar operation was carried out in the right frontal sinus with good evacuation of pus. By December 8 he developed tenderness and swelling along the midline of the lower forehead that progressed to a right frontal abscess (Pott's puffy tumor) and was drained Dec. 12, 1943. The frontal abscess was drained again December 28 and at that time x-rays showed the

typical moth-eaten appearance of osteomyelitis. Because of his continued downhill course he was transferred to Bushnell General Hospital for penicillin Jan. 10, 1944. He had received 272 Gm. of sulfonamide drugs during this time.

Fig. 8.—K. D. Case 2. Admission photograph, Jan. 11, 1944, showing draining fron-sinus prior to penicillin therapy.

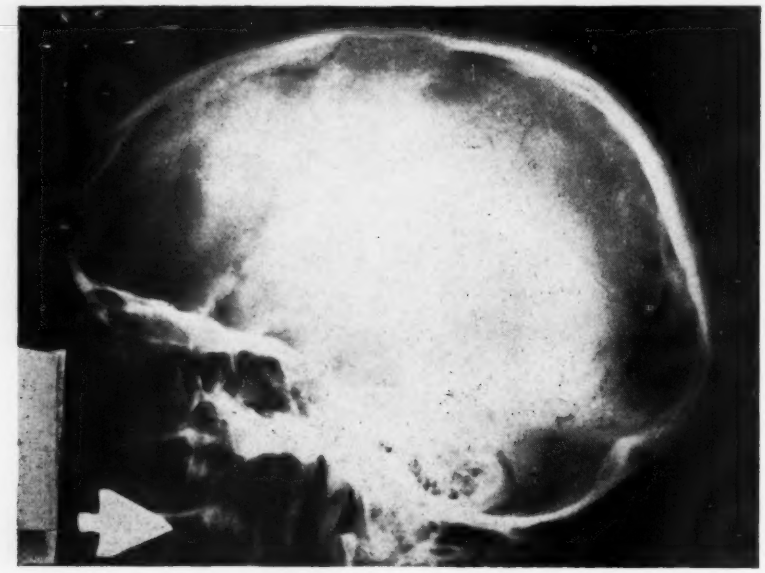


Fig. 9.—K.D. Lateral view of skull, preoperative, showing area involved by osteo-myelitis. (Jan. 20, 1944.)

Examination on admission showed a thin, emaciated middle-aged man acutely ill and complaining of severe frontal headaches. There was a linear incision over the right supraorbital ridge draining frank pus. There was also tenderness in the low mid-frontal region, but no edema or induration. A detailed neurologic examination was entirely normal except for an early proptosis of the right upper eyelid. No evidence of intracranial extension was demonstrated.

Laboratory studies showed red blood cells, 3,230,000; hemoglobin, 63 per cent; white blood cells, 9,900; polymorphonuclears, 64 per cent; lymphocytes, 36 per cent;

plasma protein, 7.2 Gm. per cent. X-ray views showed extensive inflammatory thickening of the lining membranes of all air cells. There was extensive osteomyelitis of the frontal bones on both sides of the midline, but more extensive on the right. We feel the amount of destruction has increased, especially in the direction of the vertex and involves both the inner and outer table. Culture of the draining sinus showed aerobic nonhemolytic streptococci and nonhemolytic *Staphylococcus albus.*

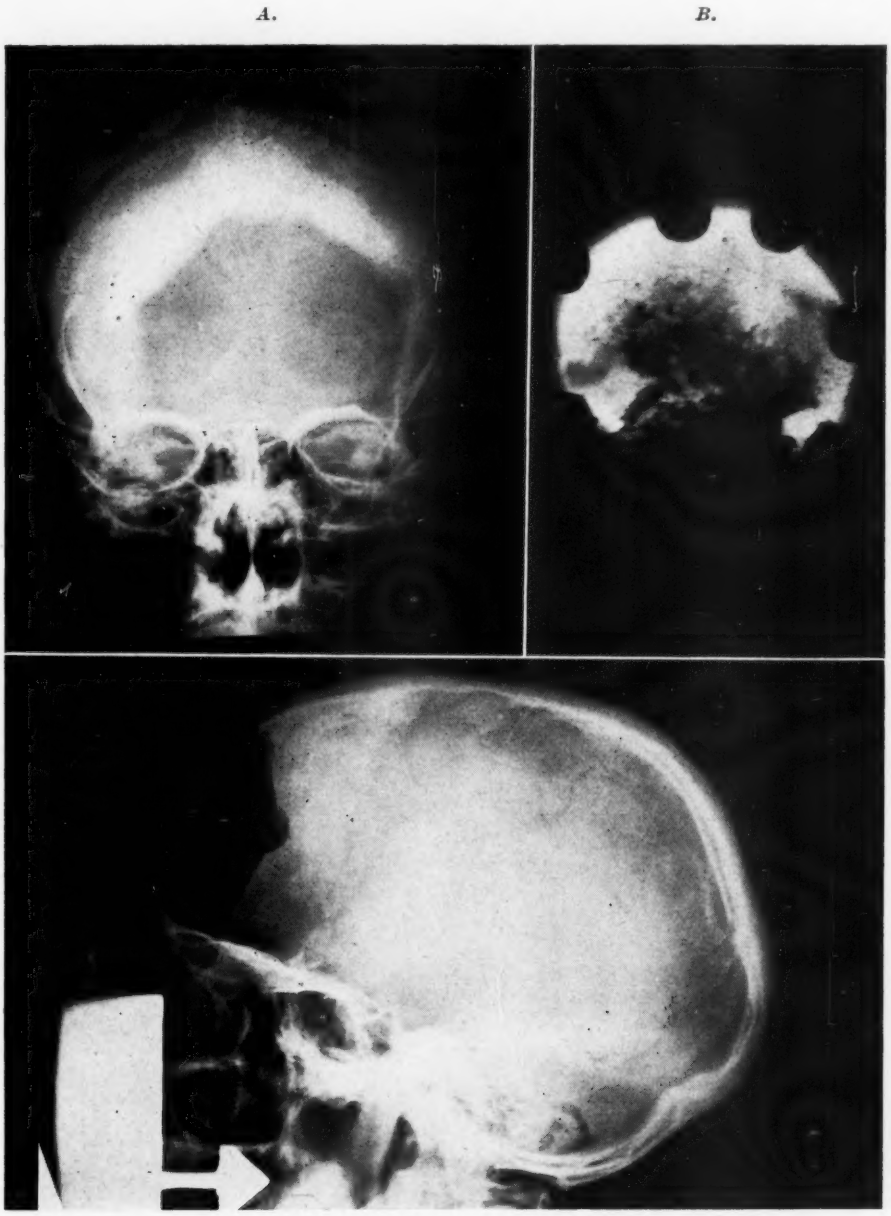


Fig. 10.—K.D. Anteroposterior (Dec. 7, 1944) and lateral (Jan. 31, 1944) postoperative views showing skull defect after removal of osteomyelitic area. Also photograph showing the involved bone removed (Jan. 22, 1944).

Diagnosis on admission was acute, nonfulminating, osteomyelitis of frontal bone, secondary to chronic pansinusitis. (Figs. 8 and 9.)

Course in Hospital.—Following determination of basic laboratory studies he was started on penicillin intramuscularly, receiving 200,000 units per day as well as local penicillin to the draining sinus. An ulcer diet was given in addition to ferrous sulfate. By Jan. 20, 1944, the drainage from the sinus incision had

stopped and the patient's condition was considered good for surgery. He had received a total of 2,000,000 units of penicillin with excellent bacteriostasis.

Jan. 22, 1944, through a coronal incision, the entire osteomyelitic area in the frontal bone was removed in one piece, and in addition, the medial half of the

A. *B.*

Fig. 11, *A* and *B*.—K.D. Postoperative anteroposterior (Feb. 26, 1944) and lateral (Feb. 2, 1944) photographs showing depression of forehead due to loss of bone.

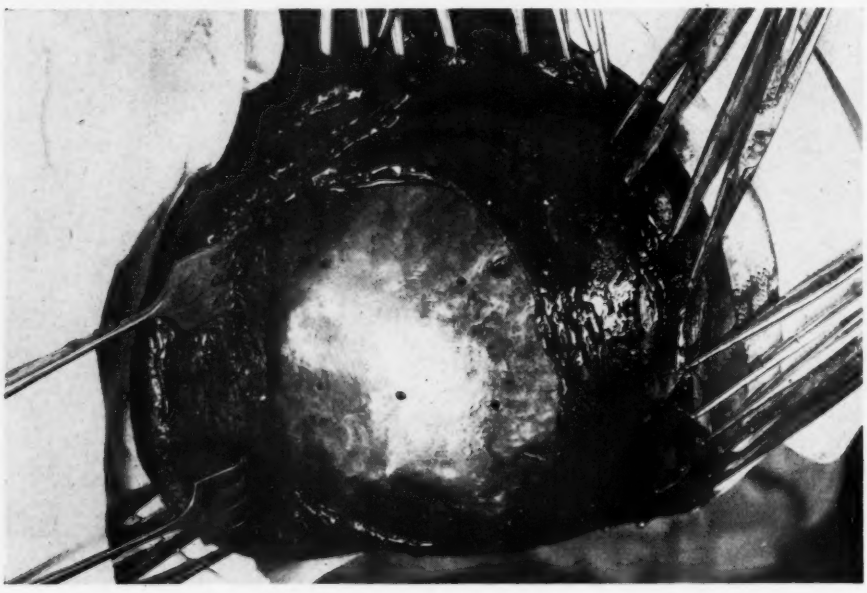
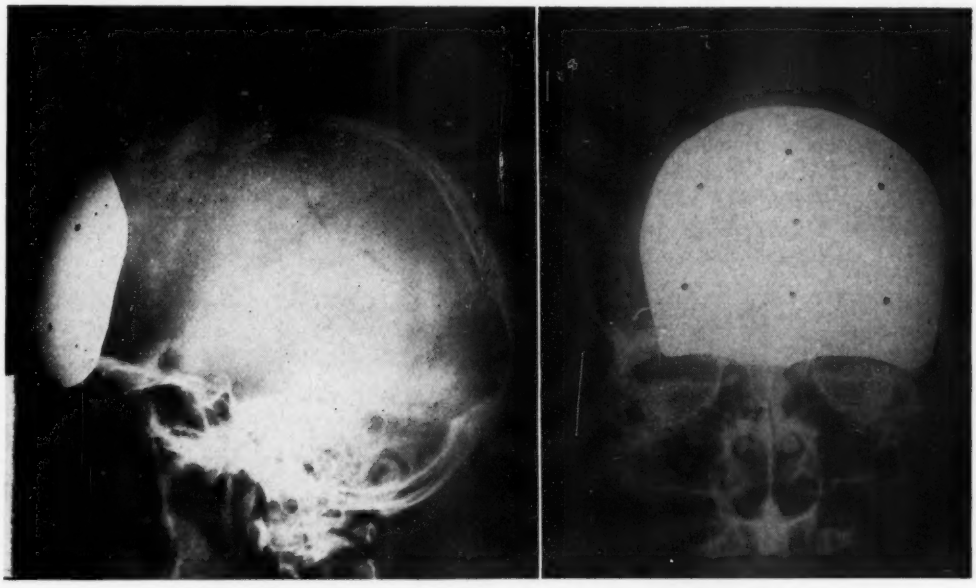


Fig. 12.—K.D. Tantalum plate (June 16, 1944) wired in place with tantalum wires. (The rakes are elevating the forehead scalp above the eyes.)

right supraorbital ridge. There was no evidence of extradural granulation tissue or pus. The frontal sinuses were also exenterated. The wound was closed without packing, but a small catheter was inserted through a stab wound for the purpose of continuing local instillations of penicillin. This was continued for four days only because the serous drainage was sterile. The incision healed per primum and he made an uneventful recovery. (Figs. 10 and 11.)

The postoperative defect was very evident and so he requested a plastic repair. A tantalum plate was prepared from a mold of the defect and on June 16, 1944, the plate was wired over the defect with a good restoration of the forehead contour. (Figs. 12, 13 and 14.)



A. *B.*

Fig. 13, *A* and *B*.—Anteroposterior and lateral x-ray views showing the tantalum plate in place (June 27, 1944).

A. *B.*

Fig. 14, *A* and *B*.—K.D. Final anteroposterior and lateral photographs showing restoration of contour of forehead and healing of all wounds, June 29, 1944.

This soldier is now feeling very well and would like to return to full duty. However, he will have to be discharged from the service because of a duodenal ulcer.

CASE 3.—E. C. M., aged 20 years, was admitted to Bushnell General Hospital March 25, 1944. This soldier had a negative history until the present illness.

On March 1, 1944, he developed an upper respiratory infection that he considered just an ordinary cold. However, on March 6, 1944, he experienced sudden severe pain over the left eye, accompanied by chills. On admission to a station hospital, March 8, 1944, examination proved negative except for tenderness on pressure over the left sinus region and redness and swelling of the left upper eyelid. The diagnosis of acute left frontal sinusitis was made and he was treated with nasal shrinkage, ice packs, sedatives, and sulfadiazine, having received 36 Gm. of the sulfonamide drug in six days without improvement. The white cell count was 15,100 with 91 per cent polymorphonuclears and on March 10, 1944, x-ray pictures of the sinus showed a bilateral pansinusitis with a fluid level evident in the left frontal sinus. By March 23, 1944, he developed severe left frontal headaches, early bilateral papilledema, left facial weakness, and a partial ptosis of the left eyelid. There was no evidence of edema of the frontal scalp on the left side. He was transferred to Bushnell General Hospital, on March 25, 1944, for treatment of a suspected left frontal lobe brain abscess.

Fig. 15.—E.M. (Case 3) Anteroposterior preoperative x-ray picture of skull showing involved area of osteomyelitis in left frontal region.

Examination March 26, 1944, showed the patient moderately drowsy and acutely ill. Temperature was 102.2° F., pulse 84, and respirations, 24. Complete neurologic examination was entirely negative except for the early ptosis of the left eyelid, mild left facial weakness, bilateral papilledema of two diopters, and generalized hyporeflexia. The only evidence of possible intracranial extension was the papilledema. Lumbar puncture showed an initial pressure of 360 mm. water. Twenty-five cubic centimeters of clear colorless fluid were removed until the final pressure was 140. The fluid contained 1 cell per cubic millimeter, total protein 30 mg. per cent, sugar 117, and cultures were negative. Roentgenograms taken April 3, 1944, showed extensive osteomyelitis of the left frontal bone, extending back to the coronal suture. There was diffuse clouding in the left frontal sinus, both ethmoids, and bilateral antral involvement. Laboratory studies showed red blood cells, 3,860,000; hemoglobin, 86 per cent, white blood cells 17,600; polymorphonuclears, 73 per cent; lymphocytes, 27 per cent; plasma protein, 6.8 Gm. per cent. Blood cultures were negative.

Diagnosis was chronic suppurative left frontal sinusitis and acute osteomyelitis of the left frontal bone. (Fig. 15.)

Course in Hospital.—Following completion of basic studies, March 30, 1944, he was started on systemic penicillin, 200,000 units daily intramuscularly for thirteen days. April 4, 1944, after he received 1,200,000 units of penicillin, a radical left external frontal sinusotomy was done. In addition, a needling of the left frontal lobe of the brain was done with negative findings. Cultures made of the sinus membrane and pus were sterile. The wound was irrigated with local penicillin for

Fig. 16.

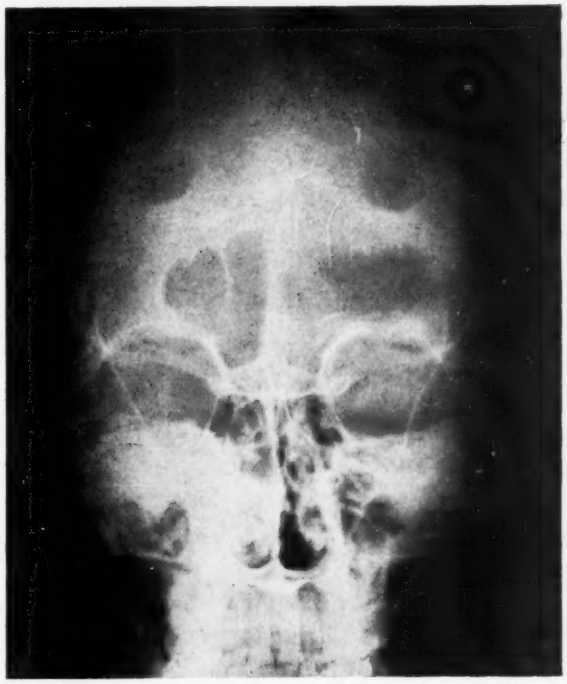


Fig. 17.

Figs. 16 and 17.—E.M. Fig. 16 is a ventriculogram, April, 1944, showing shift of ventricles. Fig. 17 is a final ventriculogram, July 8, 1944, showing the postoperative defects of left frontal sinus with osteomyelitis all healed.

five days when the wound healed. He improved sufficiently so that penicillin dosage was decreased to 120,000 units daily until April 11, 1944, when it was stopped. The headaches subsided, but the papilledema persisted, so that on April 15, 1944, a ventriculogram was done which showed a shift of the anterior horns of the ventricles toward the right, indicating a space-occupying lesion in the left frontal lobe, probably an abscess. The left frontal lobe was again needled through a postfrontal burr hole, with negative findings. Spinal fluid studies at this time showed 40 cells; polymorphonuclears, 30 per cent; lymphocytes, 70 per cent; total protein, 40 mg. per cent. Cultures and smears were negative. By May 5, 1944, x-ray pictures of the skull showed the infection to be subsiding in the left frontal bone, and the bony structure in this area appeared to be recalcified. By May 18, 1944, the papilledema had subsided completely. He was sent on a thirty-day therapeutic furlough and July 10, 1944, he was well and ready to return to duty. Spinal fluid examination was normal, July 12, 1944. (Figs. 16 and 17.)

Comment.—This patient with an acute, nonfulminating osteomyelitis had apparently received sufficient penicillin prior to operation so that all cultures were subsequently sterile and the causative organism in the sinus was not determinable. The pathologic alteration in the left frontal lobe was presumably an edema associated with the long infection. Finally it appears that penicillin may have been bactericidal in this case, although it is well known that some cases of osteomyelitis due to an organism of low virulence heal spontaneously.

DISCUSSION

In such a serious surgical disease as osteomyelitis of the frontal bone, secondary to sinus infection and of staphylococcal origin, the treatment with penicillin is revolutionary in that it controls the infection very promptly. In cases in which sequestrum formation is taking place, surgical removal of the diseased bone must be carried out in addition if a complete cure is to be effected. As reported by Lyons,[9] and also shown in Case 3, penicillin may effect subsidence of osteomyelitis in flat bones more readily than in long bones, without surgical intervention in the absence of sequestration.

It is felt that penicillin should be regarded as a bacteriostatic agent and not wholly bactericidal, particularly in bone infections of staphylococcal origin.[7] Penicillin quickly limits the spread of infections permitting early surgical removal of the infecting nidus. This was well demonstrated in the early treatment of one patient (Case 1), when we had high hopes of curing him by penicillin alone, only to learn later that surgical removal of the extensive osteomyelitis was necessary. Furthermore, there is an optimum time following treatment with penicillin when surgery must be carried out to remove the infection. If treatment with penicillin is carried on over too prolonged a time, the infecting organisms may become penicillin-resistant so that control of the infection by this agent is lost.[9]

In making a comparison of the efficacy of sulfadiazine and penicillin in these three cases, it is evident that all three patients have responded very little to the sulfonamide drug, although the adequacy of dosage may be questioned. The response to penicillin was dramatic in that all evidence of purulent discharge had disappeared completely within fourteen days in all the cases, although the drug was continued longer, hoping to eradicate the infection without operation. Cultures made prior to operation for removal of the osteomyelitic process were

sterile in all the cases, permitting primary closure of the wound in each instance. Following the use of penicillin in cases requiring surgery, we feel that use of a coronal incision with the turning down of the entire forehead and removal of the osteomyelitic area in one piece and then primary closure is definitely preferable to the formerly used inverted T incision, open packing of the wound, and the resulting deforming scar.[2, 14]

The correction of a defect in the skull depends upon the size of the deformity, its location, and the patient's concern about a "soft spot" on his head. Since the deformity of the forehead, not covered by hair, is most conspicuous, the patient is usually eager to have it corrected. We have used tantalum plate for covering the defect and find it very satisfactory. In view of the efficacy of penicillin in controlling infection, the question arises whether a plate should be prepared prior to the primary operation and be inserted at the time of removal of the osteomyelitic area, attempting to avoid a secondary operation. We think this should not be done for three reasons: first, the measurements and conformity of the plate would be indefinite as the actual defect can be determined at operation only; second, closure of the nasofrontal duct by healing granulation tissue is necessary after the primary operation to prevent recurring infection into the defect; third, large sheets of tantalum act as foreign bodies promoting infection in an already infected field even with the concomitant use of penicillin. Therefore, we advocate waiting at least three months following the primary operation and complete healing of the wound before completing the secondary plastic repair.

PREPARATION AND INSERTION OF THE TANTALUM PLATE FOR DEFECTS OF THE SKULL

Tantalum is the seventy-third element in the series 5 periodic table with a density of 16.6 and virtually no electrogalvanic action. It is very resistant to corrosion and chemical attack and has the necessary properties of malleability and ductily to lend it to a simple technique of fabrication. The .015 inch sheet tantalum is ideal for forming plates to correct the defects of the skull. Per square area, the prepared plate is but slightly heavier in weight than the bone which it replaces, weighing 1.52 Gm. per square centimeter.

The preparation and insertion of the tantalum plate offers a wide range of choice to the surgeon. The preferred method is usually the one-stage operation which requires the fabrication of the plate previous to operation, by the indirect technique. The two-stage procedure necessitates the preparation of the bone ledge around the defect, and a direct impression of the mortise joint and the surrounding bone with later insertion of the plate after fabrication. The technique for swaging the plate is the same in either case.

The preferred impression material to be used in either method is the hydrocolloid type because of its accurate reproduction of detail of the defect and the surrounding skull or scalp contour. It lends itself to use over the scalp or bone equally well and may be sterilized in the autoclave and cooled to 98.6° F. for use. Dental impression compound or the algenate impression material may be used for smaller defects but is not as readily sterilized or as readily manipulated as hydrocolloid.

To prepare the hydrocolloid impression material, we use the following formula:

Agar	62 Gm.
Green soap	5 Gm.
Magnesium sulfate	3 Gm.
Cellulose fibers from 2 sanitary napkins	
Water	1,500 c.c.

The mixture is heated in a double boiler until it is of a smooth consistency, and cooled to 120° F. for impressions over the scalp. (It may be autoclaved and cooled to 98.6° F. for impressions of the bone in direct impression, using sterile technique.)

In the indirect method, which has been used in the cases discussed, an accurate impression of the scalp and orbital ridges is made after the margins of the defect are outlined by palpating the bone edge and marking it with an indelible pencil. The area to be reproduced by the impression depends on the size and location of the defect. Ordinarily, in areas where bilateral symmetry is important, or in the reproduction of the orbital ridge, a large impression, taking in the surrounding contour and the opposite side, is helpful in establishing the corrected contour of the defect in wax.

To faciltiate removal of the impression and to limit the flow of material on application, a cardboard base (matrix) is made by cutting a hole in a suitable piece of heavy cardboard so that it fits on the skull around the defect like the brim of a hat without the crown. With the cardboard matrix in place, the impression material is painted over the defect and surrounding contour with a brush to a thickness of about one inch, care being exercised to prevent any air being trapped between the defect and the material. The hydrocolloid is then chilled for fifteen minutes by covering with towels soaked in ice water, and is then reinforced by a layer of plaster of Paris.

When the impression is "set" it is removed with the cardboard, the outline of the defect is traced with a knife blade over the marked outline, and the impression is then poured in dental stone. This reproduces the area in a master model that is an exact replica of the original defect, the edges of the defect presenting a beaded line. (Fig. 18.)

The defect in the stone model is then filled with dental wax and contoured with a heated spatula to correspond to the desired contour of the normal scalp. In all defects it is advisable to overcorrect the contour slightly, since the scalp becomes flattened over the defect and the plate is slightly depressed in its bed of bone. This corrected model is next reproduced in dental stone, Hydrocal, or Hydromite,* with the margins extending well beyond the desired edges of the tantalum plate to be made. A die and counterdie are then prepared of the selected stone by investing the die in the bottom half of a metal flask. Dental prosthetic flasks may be used for small plates, and flasks may be made of six-inch pipe for larger ones by welding in covers and guides for closing. It is important that a "lock edge" be prepared beyond the defect margin by preparing a somewhat abrupt downward contour or beaded line of the stone surface in order to "lock" the edges of the

*U. S. Gypsum.

tantalum plate while the stretching of the middle body of the plate is being accomplished. This, in short, gives an actual elevation of an area outside of the defect on the die. When the models have been well flasked, the tantalum plate (.015 inch thick), cut to approximate contour, but 1½ inches oversize, is placed properly and the two halves of the flask are closed gradually within a cylinder, pressure being applied by means of a hydraulic jack in a pressing frame, or by means

A.

B.

Fig. 18, *A* and *B*.—K.D. Photographs, May 4, 1944, showing moulages with the wax model in place and out of position.

of a large vise. The pressure must be applied gradually and evenly, allowing the metal to stretch. After closing the flask slightly, when molding has begun, it is wise to remove the plate from the flask to inspect it for wrinkles in the metal near the borders. The edges of excess metal may be trimmed off and if wrinkles are developing, they should be hammered out with a large ball peen hammer, working in the excess metal. A small hole may be drilled at the apex of the wrinkle and the wrinkle cut out producing a slit if it cannot otherwise be eliminated. By replacing this plate in the flask and press and gradually increasing the pressure until the flask is closed, periodically inspecting the plate and trimming the edges until the exact contour of the die is obtained, a very accurately fitting plate is accomplished. No great amount of work should be necessary with the hammer if the flasking operation is done properly and the initial plate is allowed to "stretch" while being securely locked at its margins. The plate should not be heated or annealed to mold it as it becomes brittle due to oxidation in open air. In the making of smaller plates, it is advantageous to make the die and counterdie of lead and zinc within a dental flask. This provides an excellent swaging surface of great strength, although the stone is entirely satisfactory if an adequate flask is provided. The method* utilizing the female die and a heavy rubber pad in pressing cylinder gives excellent results. However, the procedure just outlined affords quite satisfactory plates with a minimum of equipment and expense. After a satisfactory swaging of the plate has been accomplished, the edges are prepared to a smooth contour, having the plate slightly oversize so that it can be trimmed by the surgeon at the operating table. The plate is then boiled in concentrated hydrochloric acid for twenty minutes to clean it thoroughly. It is sterilized by ordinary autoclaving. (Fig. 19.)

Where a plate is made to close a defect tightly, small holes of 3 mm. diameter are drilled in the body of the plate to allow escape of fluid from beneath the plate in the skull so that it can be aspirated easily from beneath the galea.[14] This can be used to good advantage also should an infection supervene with the plate in place so that penicillin could be injected beneath the galea and so reach both sides of the plate.[11] The perforations also allow granulation tissue to grow through the plate between the dura and galea and so obliterate the dead space beneath the plate and help to anchor it securely in its bed.

In carrying out the second stage operation for the insertion of the tantalum plate, the patient is prepared as for an osteoplastic craniotomy under general anesthesia. The scalp is turned down over the defect, care being exercised to stop all oozing from the galea at the start so that an absolutely dry field is insured when closing the flap. The periosteum along the edge of the bone defect is then stripped back about one-half inch and the tantalum plate placed over the defect as a trial fit. The plate is cut down to proper size with a heavy curved (blunt uterine) shears, allowing an overlaying margin of about one-fourth inch. A convenient method of obtaining an accurate size plate is to mold a piece of moistened cottonoid sheet into the bony defect

*Method suggested by the Fansteel Metallurgical Corp., Chicago, Ill.

and then cut out the pattern of the defect. This pattern is then placed onto the underside of the plate, which can then be trimmed to correct size. With the plate cut to proper size, it is replaced on the skull and its margin marked with a sterilized lead pencil onto the skull. Then by means of a bone chisel 2 mm. wide (long bevel), a channel is cut through the outer table of the skull about 1 mm. deep, and the intervening outer table between the defect and this channel chiseled out by means of a bone chisel 5 mm. wide. This forms a ledge into which the plate fits securely and so prevents lateral movement. The plate can then be anchored in its bed by one of two methods. Small triangular swedges made of tantalum (.020 inch thick) can then be driven over the edge of the plate into the bone ledge in the same manner that a pane of glass is fastened into a window frame. The technique that we prefer is that of anchoring the plate by tantalum wire (.020 diameter) in four or six places, depending on the size and shape of the plate. We feel that the

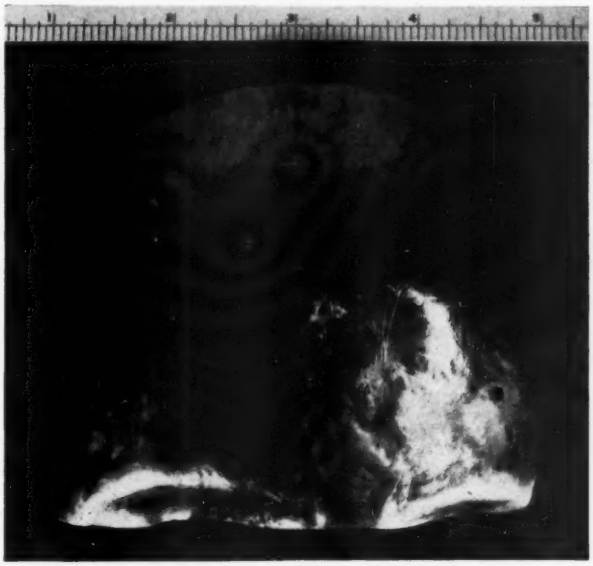


Fig. 19.—K.D. Photograph, May 18, 1944, of finished tantalum plate prior to its insertion.

plate is fixed more securely by this latter method and by turning the wire-twist ends down into the skull perforations, a very smooth fixation is effected, leaving no irregularities to be palpated through the scalp. The field is then dried thoroughly and the scalp closed in two layers with fine silk sutures. A fairly heavy compression dressing is then applied to prevent fluid accumulation about the plate. Nevertheless, on the first postoperative dressing done in twenty-four to thirty-six hours, a brain needle is passed beneath the galea and about 10 to 20 c.c. of serosanguineous fluid can be removed. The patient can usually be allowed out of bed on the third day and the sutures removed on the fifth day postoperatively. Healing is sufficiently complete in one month that the individual can carry on any average activity.

The two patients who had tantalum plates inserted into the forehead found that their hats fit them as well after operation as before they became ill. The patient with the largest plate submitted himself for placing of ice packs to the forehead to determine effects of extreme

low temperature on the plate, and he experienced no great or peculiar discomfort. He has recently been exposed to the hot sun also without any unusual effects.

SUMMARY AND CONCLUSIONS

1. Osteomyelitis of the frontal bone, secondary to sinus infection, is a serious surgical disease because of the difficulty in limiting spread of the infection. The causative organism in most cases is the *Staphylococcus aureus* or *albus*.

2. Penicillin is an excellent bacteriostatic agent in these cases so that the infectious process is brought under control rapidly, permitting early surgical removal of the diseased bone. Penicillin is not a substitute for surgery in this condition.

3. Surgical excision of the diseased bone is necessary in most instances. It can be done as soon as the infection is controlled by penicillin, at which time primary closure of the scalp is a feasible procedure. This method of treating frontal osteomyelitis is revolutionary and is the treatment of choice.

4. A small percentage of patients may recover under penicillin alone, but their progress must be observed carefully lest the process flare up again at a later date and/or the patient become penicillin-resistant which would eliminate its future use in that particular infection.

5. The correction of the postoperative defect in the frontal bone and glabella region is carried out preferably at a secondary operation, at least three months after the primary operation. This allows complete eradication of the infection in the frontal sinus region as well as complete closure of the nasofrontal duct by granulation tissue.

6. We have found tantalum plate (.015 inch thick) very satisfactory for use as an alloplastic method in the restoration of the normal contour of the frontal bone. This metal can be molded or pounded in the cold state and made to cover the defect smoothly and solidly. The plate causes no discomfort to the patient.

7. A method of preparation of tantalum plate, using dental materials, and its insertion to cover a large defect in the frontal bone has been described.

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RADICAL DUODENOPANCREATECTOMY

Report of a Successful Resection of a Carcinoma of a Duodenal Diverticulum Involving the Head of the Pancreas

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(From the Clinic)

SURGICAL lesions of the pancreas have been receiving increasing attention within the past few years. Removal of a portion of or even the entire gland has been found to be compatible not only with life but even with good health. Many of the problems concerned with the metabolism of fats, proteins, and carbohydrates have undergone and are undergoing intensive study, resulting in drastic changes in many instances in our concept of the relationship between the pancreas and our body economy. Some of the physiologic properties of this organ are still shrouded in doubt, but on the whole no more brilliant discoveries in the entire annals of medicine can be cited than those related to the functions of the pancreas.

It may be of interest to mention briefly a few of the outstanding contributors who have increased our knowledge of this organ.

To Bernard,[1] in 1856, goes the honor of being the first to classify the actions of the pancreatic juice in food digestion.

Langerhans,[2] in 1869, while still a medical student in Berlin, gave the first accurate histologic description of the pancreas and to him goes the distinction of first differentiating between the cells, which have subsequently borne his name, from those of acinar tissue.

Von Mering and Minkowski,[3] in 1889, first demonstrated the exact role of the pancreas in carbohydrate metabolism and its relationship to diabetes as demonstrated experimentally in pancreatectomized animals.

To Banting and associates,[4] in 1922, goes the honor and credit and gratitude of thousands, now and yet to come, for the brilliant discovery of insulin and its production in a form to be used in successfully controlling diabetes.

These are the men who were the outstanding contributors in the earlier study of the metabolic activities of the pancreas and who laid the groundwork which subsequently made it possible successfully to approach this organ surgically. One can state with a considerable degree of pride that most of the

Received for publication, Feb. 3, 1945.

pathologic and surgical contributions to this field have been made by Americans, or at least by those residing in the Western Hemisphere.

In 1889, Fitz[5] of Boston gave the first clear and concise description of the clinical entity of acute pancreatitis and Opie,[6] in 1903, was the first to observe a stone obstructing the ampulla of Vater and to surmise that bile shunted into the pancreatic ducts was a likely etiologic factor in acute pancreatitis.

Harris[7] of Atlanta, undoubtedly a keen clinical observer, in 1924, drew attention to the close similarity of the picture of insulin shock as observed in the overtreated patient with diabetes to the syndrome of hunger, weakness, tremor, tachycardia, convulsions, and coma associated with a low blood sugar level observed in those who do not have diabetes and relieved by carbohydrate administration. He suspected, but did not prove, that this clinical picture resulted from hyperactivity of islet pancreatic tissue.

It remained for Wilder and associates[8] of the Mayo Clinic, in 1927, and W. J. Mayo as the surgeon to demonstrate a carcinomatous lesion of the islands of Langerhans as the etiologic factor in the causation of spontaneous hyperinsulinism.

In 1929, Howland and others[9] reported the first successful removal, by Graham of Toronto, of a tumor of islet tissue from a patient with symptoms of hyperinsulinism.

These observations and experiences have led to a quickening interest in this new field of endocrine surgery so that now the literature is replete with reports of many brilliant successes following this method of therapy.

Surgery of the malignant acinar growths involving the pancreas, more particularly those of the head, in association with the common duct, the duodenum, and the papilla of Vater, is not a new concept, since Kausch[10] in 1912, reported the first successful removal of such a lesion.

Halsted,[11] in 1899, had successfully dealt with a lesion of the ampulla of Vater by resection of the duodenum with end-to-end anastomosis and reimplantation of the common and pancreatic ducts into the duodenum.

However, one need but recall the words of Sir Berkeley Moynihan[12] as late as 1926, to realize what strides forward have been made in pancreatic surgery in comparatively recent years. At this time he stated, "The radical treatment of malignant disease of the pancreas by the surgeon can hardly be said to exist," and, speaking of the attempts that had been made up to this time, "They all serve to show that the mechanical difficulties of the operation are well-nigh insuperable and that if boldness and good fortune are the operators' gifts, the result to the patient hardly justifies the means."

It has remained for those interested in the subject in recent years to make such procedures sufficiently safe and successful to be of practical significance.

Whipple,[13] in 1940, was the first to carry out successfully a one-stage radical duodenopancreatectomy. To these later surgeons and investigators who have aided in making such a procedure one that can be looked upon with favor, one must add the names of Dragstedt, Brunschwig, David, Hunt, Cattell, and many others.

Not only has improved knowledge concerning the physiologic activities of the pancreas been a contributing factor to these developments but all the other improvements that have added to the safety of surgery in general. The means at our disposal of preventing and treating shock, the use of vitamins, particularly vitamin K, in these patients who are usually jaundiced from obstruction of the common duct, the use of Wangensteen suction, the prevention

of infection by sulfonamides and penicillin, and improved methods of anesthesia are the important advances made in recent years.

Since at least a working familiarity with the known physiologic functions of the pancreas is a prerequisite to the intelligent application of surgical principles in pancreatic surgery, a brief résumé of this subject is presented at this time.

The sole functions of the pancreas, as far as are known at present, are in connection with digestion, absorption, and metabolism of fats, starches, and proteins by the medium of its internal and external secretions.

The amount of pancreatic secretion depends upon variable factors and fluctuates between 500 and 1,500 c.c. daily. It is a clear alkaline solution with a pH varying between 8.71 and 8.98, the alkalinity being largely due to the presence of sodium carbonate. Its digestive action depends upon the presence of three groups of enzymes; proteolytic, amalytic, and lipolytic in nature. The proteolytic enzyme is secreted in a zymogen or proenzyme form, trypsinogen, which is activated or converted to trypsin by something contained in the enteric mucous membrane. Pavlov supposed this substance to be an enzyme and called it kinase or enterokinase, which by hydrolytic action upon the trypsinogen converts it into trypsin. Trypsin, together with another enzyme, erepsin, acts to split the protein molecule into amino acids.

The carbohydrate-splitting enzyme, amylase, hydrolyzes starch, producing maltose and acrodextrin, which are further broken down by the maltase of the intestinal secretions to form dextrose.

Fat is hydrolyzed and saponified by lipase and broken down in the process into glycerin and fatty acids, being aided and abetted by the presence of bile.

The principal internal secretion of the pancreas, as is well known, arises from the beta cells of the islands of Langerhans, consists of insulin, and is responsible for the metabolism of carbohydrates.

Recently, Dragstedt[14] has, in his opinion, though this has not been concurred in by all investigators, demonstrated another internal secretion of the pancreas to which he has given the name of lipocaic because, as he says, it has to do in a general way with the utilization of fat. It had been his observation, along with others, that completely depancreatized dogs did not live long even though their diabetes was satisfactorily controlled with insulin. At death the most obvious autopsy change noted was extensive fatty infiltration and degeneration of the liver. Addition of raw pancreas to the dogs' diet prevented or diminished markedly these degenerative liver changes and resulted in longer survival of such animals. This was not noted when the animals were fed pancreatic secretion. A fat-free alcoholic extract of pancreas was found to have the same beneficial effect, so it was concluded that a new and hitherto undescribed internal secretion or hormone had been isolated, possibly arising from the alpha cells of the islands of Langerhans. A few scattered reports have appeared in the literature indicating that the use of lipocaic in human diabetics has been beneficial in preventing fatty degeneration of the liver and cardiovascular changes so common in this condition.

The effect of complete occlusion of the pancreatic ducts on the incidence of fatty infiltration of the liver in experimental animals has yielded conflicting results in the hands of different workers. As is pointed out by Dragstedt, animals with pancreatic fistula do not develop fatty livers when the pancreas remains normal, indicating that fatty infiltration of the liver is not due to the absence of pancreatic juice from the intestinal tract. The presence of a moderate

degree of fatty infiltration of the liver in a minority of the animals following ligation of the pancreatic ducts seems, therefore, to be due to the atrophy of the pancreas that takes place in these animals. There is evidence that this atrophy affects the islets as well as the parenchyma in some cases. These experimental observations may help to account for the clinical variations that have been noted following surgery on the pancreas, and will be referred to later in this paper.

Tests for acute and chronic inflammatory lesions of the pancreas have within recent years been of considerable practical importance to the clinician. In the early stages of acute pancreatitis, within the first three to five days to be exact, lipase and amylase determinations in the blood and amylase in the urine usually reach high levels, sufficient to be of importance in the differential diagnosis between pancreatitis and other acute abdominal lesions. Comfort and Osterberg,[15] Whipple,[13] Fennel,[16] and others have called attention to this valuable laboratory aid. In chronic pancreatitis these determinations have not been found of value but other methods have been elaborated.

In 1902, Bayliss and Starling promulgated the secretin theory to account for the flow of pancreatic juice. It was their belief that acid chyme coming in contact with the mucosal cells of the duodenum and upper intestine changed a prosecretin into secretin. Secretin being absorbed into the blood stream stimulates the pancreas to function. In 1937, Agren and Hammersten[17] isolated the hormone secretion in crystalline form, which apparently is specific for pancreatic cells with the exception that it may augment bile secretion. When injected intravenously this substance produces a great increase in flow in the secretion of the normal pancreas. In 1939, Lagerlof,[18] using a double lumen tube, one being passed through the pylorus into the duodenum and the other remaining in the stomach, was able to aspirate pure pancreatic juice in large amounts following injection of secretin intravenously. In chronic inflammatory lesions of the pancreas this response is markedly diminished, and in obstructive lesions is absent. In jaundiced individuals this method of examination has been found of value in differentiating obstructive lesions of the common and hepatic ducts from those in the region of the papilla of Vater and head of the pancreas, obstructing both the biliary and pancreatic outflow.

According to Whipple,[13] mecholyl or methylacetylcholine has further elaborated the duodenal determinations of pancreatic ferments. Secretin, which is a hormone, increases the volume and alkalinity of pancreatic juice, while mecholyl, acting through the vagus, increases the concentration of the ferment without increasing the volume and alkalinity and is a more accurate index of the activity of acinar tissue than of the obstruction of the flow of the pancreatic juice.

This would seem to be the opportune time to discuss more fully some of the observations that have been made clinically and experimentally when the external secretion of the pancreas has been abolished by resection of the head of the pancreas and closure of the remaining stump and when both the internal and external secretion (hormone and enzyme action of the organ) has been deleted by its complete extirpation. Many of the problems associated with surgery of the pancreas were formerly of interest only to the physiologist. Much of our knowledge of the pancreas has been derived experimentally from laboratory animals, particularly the dog, but unfortunately with accumulating clinical experience the correlation with human physiology is not always applicable. However, this method has been of inestimable value. For instance, it was formerly thought that removal of the duodenum was not compatible with life. Drag-

stedt and co-workers,[19] in 1918, first successfully removed entirely this structure from the dog and this observation has subsequently lent courage to those attempting the procedure in man.

Until recently, complete removal of the pancreas in man had not been successfully accomplished. While it yet remains to be demonstrated that this is a procedure of practical importance, sufficient encouraging data have been accumulated, both experimentally and clinically, to justify further consideration and investigation.

As we have previously pointed out, depancreatized dogs do not survive long even if the resulting diabetes is adequately controlled by insulin administration. Autopsies have shown a remarkable accumulation of fat in the liver of such animals. Oral administration of from 100 to 200 Gm. of raw pancreas daily suffices to prevent this fatty change and permits these dogs to survive for long periods of time and perhaps indefinitely when their nutritional needs are adequately supplied. Raw pancreas furnishes lipocaic previously mentioned.

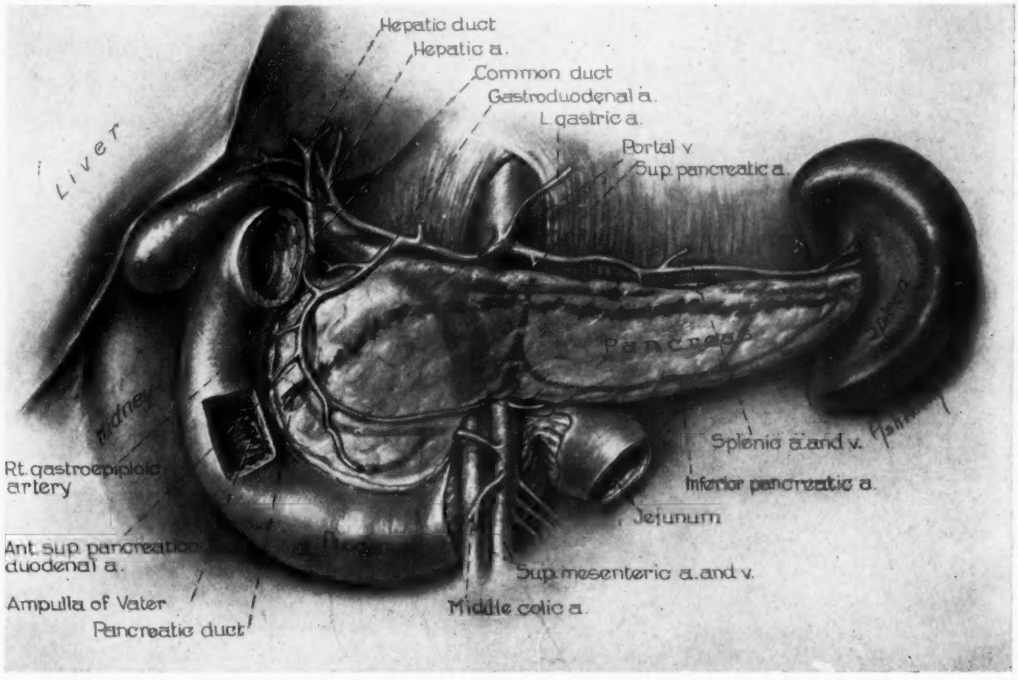

Fig. 1.—Normal anatomy of the duodenopancreatic region.

In the human being, so far as I have been able to determine, only two or three total pancreatectomies have been recorded.

Rockey,[20] in 1943, reported practically a total pancreatectomy for carcinoma, the patient surviving for fifteen days. Autopsy revealed less than 1 Gm. of pancreatic tissue remaining.

The second case was reported in February of 1944 by Priestley and associates,[21] from the Mayo Clinic, and is of special interest because the patient was alive and well at the end of sixteen months. The patient presented the typical picture of hyperinsulinism and at operation no pancreatic tumor could be identified. The entire gland, which weighed 80 Gm., was removed and subsequently an islet tumor 2 by 5 by 5 mm. was found to account for the symptoms of hypoglycemia.

It has been found both experimentally and clinically that diabetes occurs only when over 90 per cent of the pancreas is removed. This diabetes is severe

and necessitates daily administration of from 60 to 100 units of insulin in the human being to effect control. Diabetes in totally depancreatized animals is less severe and is more easily controlled than that occurring following partial resection. This was found to be the case in the two total removals in human beings. Stabilization was reached in Rockey's case at less than 27 units of insulin daily and in the case reported by Priestley the highest blood sugar level was 341 mg. per cent the morning after operation and the greatest total units of insulin administered for a single day were 66. From about the fifth post-operative day on, control of the diabetes was obtained by a single daily subcutaneous injection of protamine zinc insulin and regular insulin, averaging 30 units, the ratio being from 1 unit of protamine zinc to from 1 to 2 units of regular insulin.

In an attempt to offset the fatty changes noted in the depancreatized experimental animal the patient was fed a diet rich in choline. Fifty grams of cottage cheese of high protein content were considered adequate to prevent such changes. The excellent health of the patient sixteen months after total removal of the pancreas was thought to be good evidence that such change had not developed. From rather extensive metabolic studies no disturbance in carbohydrate digestion could be detected. From 35 to 70 per cent of the ingested fat and from 25 to 55 per cent of ingested nitrogen could be accounted for in the feces. In spite of this loss a positive nitrogen balance occurred and the patient has remained in excellent health with no evidence of deficiency of lipocaic.

Observation of many more human beings in whom the entire pancreas has been removed with favorable results will, of course, be necessary before this procedure can be considered to be of practical significance. However, this single encouraging report should do much to stimulate further interest in this subject.

In order further to present various aspects, both physiologic and technical, associated with the operation of radical duodenopancreatic surgery, it seems desirable to present the following case report and follow this by a discussion of the various problems that arose in the conduct of the case.

CASE REPORT

A 44-year-old Chinese man was first seen in consultation with Dr. K. C. Chock, July 7, 1944. The onset of symptoms occurred five months previously with upper abdominal pain and discomfort associated with diarrhea. There had been as many as six to eight stools daily and the patient had noticed the presence in them of droplets of oil, particularly following ingestion of fatty foods. During this time there had been a loss of fifteen pounds in weight. Physical examination was essentially negative except for moderate tenderness and muscle spasm to the right and above the umbilicus. It was thought that an indefinite mass could be palpated in this area. Urine examinations had intermittently shown the presence of sugar. However, the blood sugar level on June 6 was 80 mg. per cent and three days later a glucose tolerance test showed: blood sugar 102 mg. per cent, urine negative; blood sugar 166 mg. per cent, urine negative; and blood sugar 169 mg. per cent, urine showed a trace of sugar.

July 1, feces examination for determination of pancreatic enzyme deficiency showed amylase measure of digestion 400 units (normal 30,000 to 60,000). Gastrointestinal x-rays revealed a large space-taking lesion involving the region of the head of the pancreas as shown by the wide arc made by the duodenum.

Exploration of the abdomen at this time was advised, but was refused.

The patient was not seen again until Oct. 5, 1944, approximately eight months after the onset of the trouble. Symptoms remained essentially the same. He had lost five pounds more in weight, and the fatty diarrhea continued. A mass was now definitely palpable. It was significant that the patient had not had clinical evidence of jaundice at any time.

The patient was admitted to the Queen's Hospital for further study and operation. An attempt at gall bladder visualization by oral dye was unsuccessful. Intravenous pyelograms were negative.

Blood count showed: red cells 4,600,000, white cells 3,200, polymorphonuclears 48 per cent, lymphocytes 45 per cent. Red cells were normal. Hemoglobin was 81 per cent (12.2 Gm.).

Plasma protein was 6.7 mg. per cent, nonprotein nitrogen was 35 mg. per cent, fasting blood sugar was 138 mg. per cent, Wassermann and Kahn were negative.

The patient was operated upon Oct. 5, 1944, under cyclopropane-ether anesthesia. The duration of the operation was three hours and forty-five minutes. A right rectus muscle-splitting incision was made and later, to gain better exposure, the incision was carried transversely to the left above the umbilicus. A mass occupying the head of the pancreas was encountered that seemed confined to this area and for this reason was considered probably operable. Exploration retroduodenally by way of an incision through the peritoneum to the lateral side of the duodenum substantiated this opinion.

The common duct was temporarily ligated and severed at the upper margin of the duodenum. The gastrohepatic ligament and the transverse mesocolon were severed to enable the removal of the distal two-fifths of the stomach. The jejunum was severed just beyond the ligament of Treitz. The tumor, which was intimately adherent to the portal and superior mesenteric veins, was carefully dissected free of these structures. In so doing the portal vein was opened. Bleeding was controlled by plugging the opening with the index finger of the left hand while repair of the opening was made with fine interrupted silk. The duodenum was fished out from beneath the superior mesenteric vessels, the pancreas was severed wide of the tumor, and the specimen, which consisted of the distal two-fifths of the stomach, the distal one-third of the common duct, the entire duodenum, and the head and body of the pancreas containing the tumor were removed.

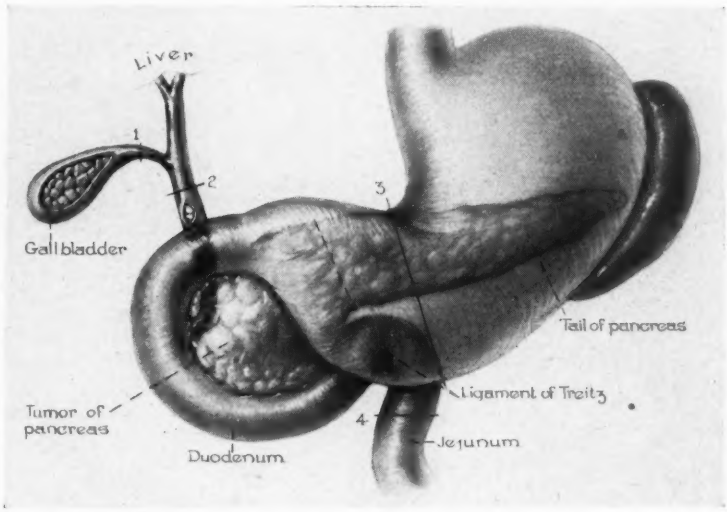

Fig. 2.—Showing the pathologic processes and the site of resection of the gall bladder, the common duct, the duodenum, the pancreas, and the stomach.

The remaining portion of the pancreas was quite firm and indurated and the duct dilated, easily admitting the end of a hemostat. The distal end of the severed jejunum was brought up behind the colon and fitted over the end of the pancreas, suturing the serosa of the jejunum to the side of the pancreas with two continuous rows of atraumatic chromic catgut and one row of interrupted silk. The same technique was used subsequently in the anastomosis of the common duct and stomach, to the jejunum. The posterior layer of peritoneum of the lesser omental sac was utilized in reinforcing the anastomosis of the duodenum and pancreas and lent itself to this purpose quite satisfactorily.

The common duct was approximately twice its normal size in diameter. The gall bladder was filled with stones. It was removed. Two small stones were found in the common duct and these were removed. No others could be found by scoop or following irrigation. The duct was anastomosed to the jejunum over the proximal flared end of a short segment of a No. 16 rubber catheter. Beyond this the stomach was anastomosed end-to-side to the jejunum. Three soft rubber tissue drains were inserted, one into the region of the common duct anastomosis and the others to the region of pancreatic anastomosis, and the incision closed.

During the operation and immediately following, the patient received 2,500 c.c. of blood. He stood the operative procedure well.

The patient was known to be sulfa-sensitive. To help offset infection he was given postoperatively 20,000 units of penicillin every three hours for forty-eight hours. Wangensteen suction was continuous for four days, then intermittent for forty-eight hours. He was given 1,000 c.c. of lactate Ringer's solution containing 10 per cent glucose plus 100 mg. of cevitamic acid, 20 mg. vitamin B_1, and 100 c.c. of 15 per cent amino acids every eight hours, for four days or during the time of Wangensteen suction.

Recovery was uneventful except that beginning on the eighth postoperative day there was considerable drainage of bile for about four days, probably due to leakage through the stump of the cystic duct. So far as could be told there was no drainage of pancreatic secretion. There was no irritation of the surrounding skin about the drain and the wound healed kindly.

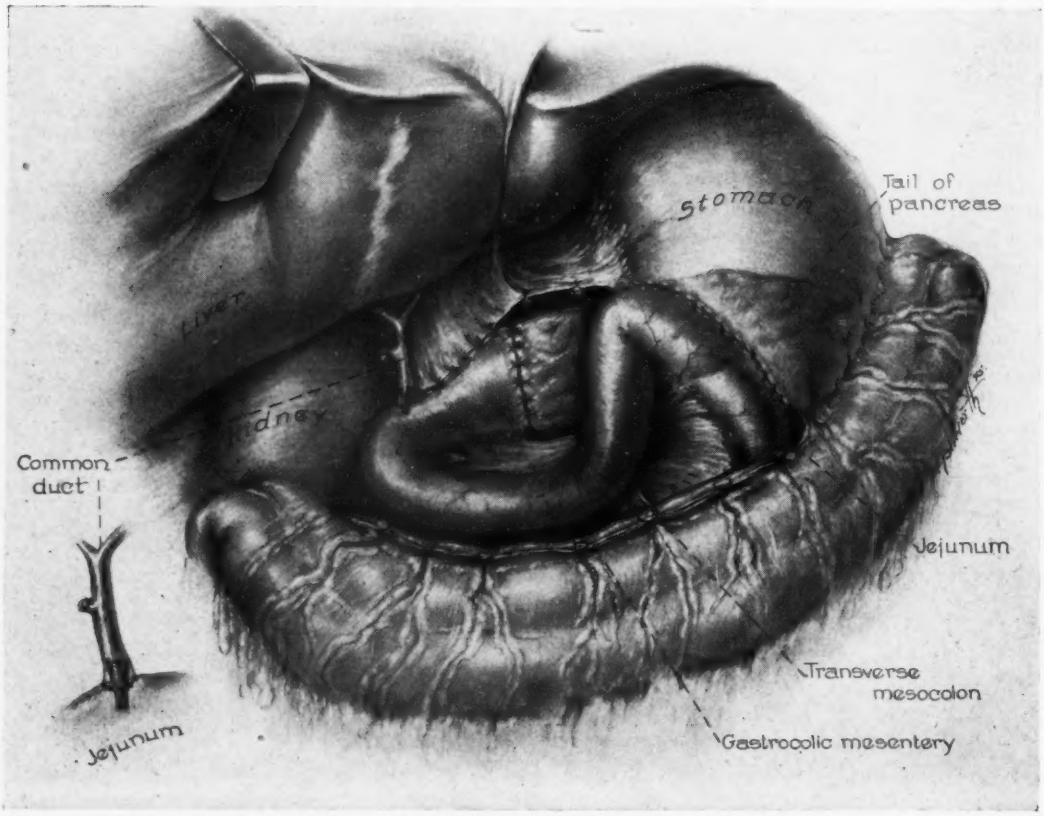

Fig. 3.—Showing the anastomosis of the pancreas, common duct, and stomach to the jejunum.

*Pathologic Report.**—

Gross: The specimen consisted of a portion of stomach measuring 12 cm. in length along the greater curvature. The mucosal markings were normal except for one small area which was raised and measured about 3 mm. in diameter. It was confined to the mucosa. There was also a gall bladder measuring 15 cm. in length. It contained bile and about sixteen calculi of mixed type, varying from 3 to 15 mm. in diameter. The wall of the gall bladder was somewhat edematous. Separately was a portion of small intestine measuring about 30 cm. in length, which was stretched over a tumor mass measuring 10 cm. in diameter. There were three large ulcerated areas which showed perforations into this mass, so that the lesion grossly was either a large diverticulum or a tumor which had ulcerated into the intestine. The ulcerations measured approximately 2 by 1 cm., another 3 cm., and the other 2.5 by 1.5 cm. Thick mucus and tumorlike tissue protruded through the ulcerations. When the specimen was incised, it showed what appeared to be a large amount of adenomatous tissue and mucus, with several long glandular pockets like that of a diverticulum, but in addition there were foci of gelatinous material closely resembling carcinoma. There was a fibrous wall surrounding the entire mass, in part at least of inflammatory origin.

*By Dr. Sumner Price, Pathologist, The Queen's Hospital, Honolulu.

Microscopic: Histologic examination of the gall bladder showed a subacute exudative inflammatory reaction, with slight hypercholesterolosis of the mucosa of the gall bladder. There was a well-marked cellular inflammatory reaction involving the mucosa, which extended down into the muscularis. There were a number of eosinophiles present, as well as a considerable number of polynuclears and lymphocytes. Examination of the stomach wall showed

Fig. 4.—The amount of stomach remaining after resection.

Fig. 5.—The gross specimen, showing probe in the common duct, the entire duodenum, the tumor involving the head of the pancreas, the gall bladder containing stones, and the resected stomach.

a small, benign polypoid adenoma, and at one point there were a few glands deeply imbedded beneath the muscularis mucosa which suggests that there was probably present a small unrecognized diverticulum of the gastric wall. A section from the duodenum showed a large diverticulum wall presenting edematous and hypertrophied villi. There was a well-marked inflammatory reaction present as well as a large amount of mucus. There were numerous glandular cells distributed throughout the wall of the diverticulum and separately there was definite evidence of an early low-grade adenocarcinoma involving the wall, showing large pockets of broken glandular tissue, with mucinous exudate, which coincided with the gross appearance of the lesion. However, new sections will have to be made from the capsule of this mass to determine the degree of infiltration of the surrounding structures and a subsequent report will be filed.

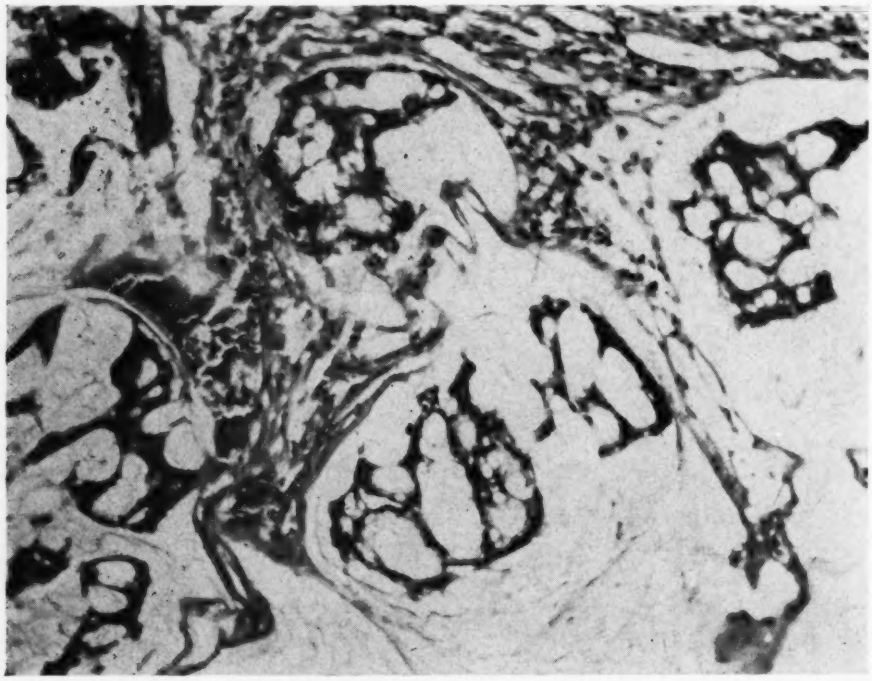

Fig. 6.—Showing the histologic structure of the tumor.

Diagnosis: Small adenoma of the mucosa of the stomach. Questionable diverticulum of the stomach. Large ulcerated diverticulum of the duodenum, with secondary adenocarcinoma.

Supplementary Report.—Histologic examination showed a thickened wall of a diverticulum from the duodenum, with foci showing adenocarcinoma. There was no question as to whether the lesion was from a diverticulum since the pockets contained villi like those found in the duodenum. In the thickened wall were found also a few elements of pancreatic tissue with general atrophy of the parenchyma. However, there was no evidence that the pancreas played any role in the tumor, and this atrophic change was a frequent finding in inflammatory and obstructive lesions in the pancreas, and had no relationship to the tumor. Separately there was a lymph gland found attached to the specimen and it presented no evidence of any metastases.

Diagnosis: Diverticulum of the duodenum with adenocarcinoma.

The patient was discharged on the thirtieth postoperative day, having remained in the hospital longer than necessary because of home conditions. The urine remained free of sugar and two months following operation the blood sugar was 106 mg. per cent. Several urine and blood amylase determinations have been within normal limits.

In the majority of lesions of the head of the pancreas in which radical resection is indicated, there is an associated jaundice due to common duct obstruction. The question then arises as to whether the operation should be done in one or two stages. With the use of vitamin K there is undoubtedly less danger to the one-stage procedure but the majority opinion, I believe, favors the cor-

rection of biliary obstruction as a preliminary procedure, particularly in debilitated subjects. Implantation of the common duct into the jejunum holds preference over other procedures. Objections to the two-stage method are the likelihood of increasing technical difficulties subsequently by adhesions and the increased danger of two anesthetics and two operative procedures, to say nothing of the objections by the patient. Since jaundice was not present in the case we are presenting, this question did not come up for consideration.

Why was two-fifths of the stomach resected?

It is well known and becoming more firmly established in the minds of those doing gastric surgery that anastomosing the jejunum to an intact stomach is followed in a high percentage of cases by gastrojejunal ulcer. These data, of course, have been accumulated following gastroenterostomy for duodenal ulcer where the gastric acidity is almost universally abnormally high. Whether this high percentage of ulcer would occur without an ulcer diathesis, of course, no one knows, since there has been no series of cases where this has been done. However, in supposedly normal stomachs in the experimental animal (the dog), again it has been shown that such ulcers do develop particularly when the external secretion of the pancreas has been eliminated from the intestinal canal.

The experiments of Mann and Williamson,[22] Elman,[23] and Dragstedt and associates[19] have shown some interesting observations in this respect. With total pancreatic fistulas, almost 100 per cent of animals probably would develop duodenal ulcers unless large amounts of alkalies were administered. This presumably is due to the absence of alkaline pancreatic secretion neutralizing the acid gastric content. In depancreatized dogs there is almost complete immunity to ulcer, Dragstedt reporting less than one dozen cases in 400 such animals. Animals with ligated pancreatic ducts occupied a midground.

It is difficult to understand why diversion of the external secretion of the pancreas from the intestinal canal is so commonly associated with duodenal ulcer while complete removal of the pancreas is so rarely followed by ulcer. Perhaps further elucidation of these findings may throw additional light on the etiology of peptic ulcer in man. Suffice to say that removal of the distal two-fifths of the stomach in our case was done in order to remove that portion of the stomach that supposedly stimulates the acid-secreting cells of the fundus. By this procedure we hope to decrease the normal gastric acid secretion and help prevent the subsequent development of a gastrojejunal ulcer.

The next question—Why was the remaining portion of the pancreas inserted into the open end of the jejunum?—can be answered by saying that we hoped to preserve some of the external secretion of the pancreas. The necessity for attempting to do this is at the moment a debatable one. Most of the data at present have been obtained from the experimental animal, though information from human beings is being rapidly accumulated following radical operations on the pancreas.

Without exception, the exclusion of pancreatic juice from the intestinal canal in laboratory animals causes the appearance of large amounts of undigested fat and protein in the feces as shown by Pratt, Ralli, and others.[24, 25] This imperfect absorption of fat cannot be accounted for entirely through failure of digestion of fat since a similar though less severe excretion of fat was found when animals were fed on fatty acids.

In human beings a similar though usually less severe disturbance in digestion and absorption of fats and protein is noted when the head of the pancreas is resected and the remaining portion is left unconnected with the gastrointestinal canal. Under these conditions there occurs a fatty diarrhea, steatorrhea,

the presence of undigested meat fibers showing transverse striatous creatorrhea, and an increase in nitrogen content of the stool azotorrhea.

Whipple and co-workers[26] found, in three patients with complete duodenectomy and total exclusion of the pancreatic juice from the gastrointestinal tract, fat digestion of 80 to 85 per cent of a carefully measured fat intake, and, in a patient who came to autopsy nine months after radical operation, fatty degeneration of the liver was not found. In only one of the five patients surviving for periods of five to twenty-eight months after radical operation have they found a disturbed fat metabolism. Rekers, Pack, and Rhoads,[27] on the other hand, did metabolic studies on a patient who had undergone a resection of the duodenum and head of the pancreas and ligation of the pancreatic ducts. Six supposedly normal individuals were used as controls. In this patient it was found that from 87 to 95 per cent of fat and from 39 to 45 per cent of nitrogen ingested was lost in the feces. They found that the addition of amino acid nitrogen to the diet did not increase significantly the fecal output so concluded that the digestion of protein and not the absorption was impaired. Daily ingestion of 6 Gm. of lipocaic was without significant effect, but the daily administration of 25 Gm. of the external secretion of the pancreas in the form of enteric coated pancreatin* caused a fall in the feces of the amount of fat ingested from 91 to 32 per cent and nitrogen from 44 to 3 per cent of that ingested. They further found that an increase in the protein content of the diet resulted in increased absorption of fat, while an increase in the fat content resulted in an increase of fat absorbed but no lessening of fat lost.

It has been found that on an unregulated diet considerable variation in fat excretion will be found in different individuals and even in the same person from day to day.

Fowweather[28] analyzed the stools of eighty hospital patients without evidence of gastrointestinal disease and arrived at the following conclusions:

1. Any specimen in which the total fat amounts to more than 25 per cent of the total dry matter is probably abnormal.

2. Any specimen in which the neutral fat exceeds 11 per cent of the total dry matter or 55 per cent of the total fat should be suspected of showing evidence of deficient fat splitting.

3. Any specimen in which total split fat (that is, the sum of soap fat and free fatty acid) exceeds 16 per cent of the total dry matter or 75 per cent of the total fat should be suspected of showing evidence of deficient fat absorption.

Kolmer[29] states that normally the daily average of fecal nitrogen varies from 1.5 to 2.3 Gm. and lipids from 7 to 10 Gm.

It has also been shown that even on a fat-free diet there is a daily excretion of about 2 Gm. of fat, the composition of which is very similar to that of blood lipids and it is now generally believed that at least a fraction of the fecal lipids is derived from the blood and is secreted into the small intestine.

Bodansky and Bodansky[30] state that on a Schmidt diet which consists of the daily ingestion of 118 Gm. of protein, 111 Gm. of fat, and 119 Gm. of carbohydrate, the normal individual will absorb over 94 per cent of the fat and over 92 per cent of the nitrogen. It is further pointed out in their studies of pancreatic steatorrhea that the maintenance of nitrogen balance may be difficult since as much as 80 per cent or more of intake of nitrogen may be excreted in the stools and that a combination of high protein intake and pancreatic enzymes are often of no avail in preventing imbalance.

*Parke, Davis & Company, Detroit, Mich.

While it would seem advisable, if possible, from the data presented, to preserve the external secretion of the pancreas in order to prevent steatorrhea, creatorrhea, and azotorrhea, and perhaps complications that we at present are unfamiliar with that may arise in cases that are observed longer, it has not been the universal custom, by any means, of surgeons to do so.

Brunschwig[31] states, after an experience with eight one-stage pancreatoduodenectomies, that the successful anatomic implantation of the pancreatic stump into the bowel in man has not yet been demonstrated to approach normal or appreciable secretion of pancreatic juice into the bowel and that he will continue to close the stump of the pancreas until it is proved that successful transplantation can be done.

Cattell,[32] on the other hand, has reported fifteen radical operations and he has been a consistent advocate of implanting the remaining stump of the pancreas into the jejunum. On his recent visit to Hawaii he stated that he had now done twenty-one such operations and still believed that the remaining pancreas should be anastomosed to the jejunum.

Child[33] reported a one-stage radical pancreaticoduodenectomy in which the stump of the pancreas was implanted into the open end of the jejunum. From secretin tests before and after operation, he concluded that there was approximately one-sixth of the normal pancreatic secretion into the intestine. The patient manifested no abnormality in fat digestion, following operation.

According to Hunt,[34] Tenani, in 1922, and he, in 1941, successfully implanted the stump of the pancreas into the open end of the jejunum. He stated that preservation of the external pancreatic secretion is desirable but that the problems of pancreatic intestinal anastomosis are great.

As Whipple[13] has stated, "It is evident that the question of disturbed fat metabolism in a patient whose pancreas is completely isolated from the gastrointestinal tract is not as yet completely answered and only a large number of patients surviving the operation from three to five years will provide the necessary data for an accurate statement in this regard. It may be necessary to renew the efforts to re-establish the communication between the pancreas and the gastrointestinal tract in the radical removal of the ampullary and pancreatic cancers."

In the case which we have reported it would seem that some benefit has accrued from implanting the tail of the pancreas into the jejunum, though too many factors enter into the picture to permit a clear evaluation. Previous to surgery the patient was having six to eight stools daily, containing much gross evidence of fat. Subsequent to operation, bowel movements had been two to four daily without gross evidence of fat. However, he has been instructed about eating a diet low in fat and he has been receiving 20 gr. of pancreatin four times daily. Analysis of the stool on this regime has shown it to consist of 78.3 per cent water and 21.7 per cent solids. Of the solid material the total fat, made up of neutral fats, free and combined fatty acids and soaps, constituted 40.7 per cent by weight of the dried residue, a definitely abnormal amount of fat in the feces, especially in a patient on a limited amount of fat intake. Examination of the stool for meat fibers has shown their presence in large numbers and microscopic examination of the stools shows many fat droplets. Pancreatin was discontinued for one week and an increasing diarrhea was noted. Fat droplets became visible grossly and microscopic examination of the stool showed an increased number of undigested meat fibers. Determination of fat in the feces showed this made up 55 per cent of the dried residue. To date we have been unsuccessful in

obtaining lipocaic. In spite of his disturbed metabolism he is gaining strength, but not weight, and has returned part time to his original work as a radio mechanic.

Technically the implantation of the remaining pancreas into the open end of the jejunum was easily done and no resulting pancreatic fistula resulted. The use of the peritoneum of the lesser omental sac in closing over the line of anastomosis seemed to add definitely to the security of the procedure. The literature contains a number of methods of anastomosing the pancreatic ducts into the intestinal canal but the procedure used as reported would seem to have definite advantages. Placing the anastomosis proximal to the inflow of bile and gastric content, I believe, adds materially to the safety of the procedure.

The method of re-establishing the flow of bile into the gastrointestinal canal has varied but it seems to be the consensus at the moment that the safest method is to implant the common duct into the jejunum. Ligation of the common duct and implantation of the fundus of the gall bladder into stomach or jejunum have resulted in a high incidence of biliary fistula due to the ligature about the common duct blowing off or the duct not healing over. If this method is to be used the end of the common duct should be inverted before it is closed. Cholecystogastrostomy has in the past resulted in a high incidence of ascending hepatic infection, partially due, it is thought, to the vigorous gastric peristalsis forcing food particles up the ducts. If the anastomosis is made to the jejunum proximal to that of the gastrojejunostomy this complication is not so likely to occur.

SUMMARY

A brief review of the present known physiologic properties of the pancreas as related to radical duodenopancreatic resection is presented.

A case of carcinomatous degeneration of a duodenal diverticulum involving the head of the pancreas, in which successful radical duodenopancreatic resection was done, is recorded. So far as can be determined this is the first successful operation for this condition reported in the literature.

A discussion of some of the technical problems encountered in this operation is indulged in.

CONCLUSIONS

With present advances in anesthesia and pre- and postoperative care, with a clearer understanding of the physiology of the pancreas and replacement therapy, and with familiarity with certain technical procedures, radical duodenopancreatectomy can be carried out with a sufficient degree of safety to justify the procedure in selected cases and with the expectation of material benefit to the patient.

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Editorial

Anesthesia

THE possibilities in anesthesia have increased perhaps tenfold in the last ten or twelve years. The respiratory and circulatory physiology may be kept within normal limits much more certainly and much more precisely than ever before. Blood levels of oxygen and of carbon dioxide may be controlled very well and are on the way to control with still more precision. Relaxation may be obtained to the point of flaccidity with a minimum of depression of the brain and spinal cord. Respiration may be controlled to the point of quietness and absence of effort without disturbing physiologic function. All this may be done with almost an absence of the postanesthetic prostration which was expected ten and fifteen years ago and occurs too often today.

The drugs and equipment which are available to help us accomplish these things have increased year after year in number and variety. Each one has its special points of value and its special weaknesses. Each should be used to accomplish the result for which it is best suited, and should not be used in an overdose to try for an effect which another drug or method can better bring about. Thus, combined or balanced anesthesia has become the true picture of today's art. Those who use today's material and equipment in anesthesia must know it well, must be skilled in its use, and must know much more clinical physiology than the anesthetists of yesterday. Without such training they must plod along with the anesthesia of yesteryear and accept the inferior results of that time.

Do all of these improvements simplify the problems of the surgeon? Not at all, unless he entrusts them to someone in whom he has complete confidence. With the old drop-ether formula he could fairly well watch the anesthesia and direct it. With the newer drugs, equipment, and methods the results in the hands of well-trained anesthetists can be unspeakably finer and more satisfying, but it seems impossible for the surgeon, when things are not going satisfactorily, to discern what the trouble or troubles may be and help to correct them while giving adequate attention to his surgery. All he can do is to ask or demand better conditions, and only knowledge and skill at the head of the table can avoid trouble or correct it if it should appear. The use of the newer armamentarium of precision, with insufficient knowledge or skill, usually leads to more confusion and dissatisfaction.

The surgeon who has not tasted anesthesia for his surgery under the best possible auspices has something to look forward to, the value of which he perhaps does not yet appreciate. A higher quality in anesthesia than the present best is surely still to be attained and never before has there been such active effort in seeking it.

—Ralph T. Knight, M.D.
Minneapolis, Minn.

Book Reviews

Pain. Research Publications, Association for Research in Nervous and Mental Disease, Vol. XXIII. Editorial Board: Harold G. Wolff, M.D., Herbert S. Gasser, M.D., and Joseph C. Hinsey, Ph.D. Pp. 468, with 116 illustrations, and 19 tables. Baltimore, 1943, Williams & Wilkins Company, $7.50.

As everyone interested in nervous and mental diseases knows, the Association for Nervous and Mental Diseases holds a meeting annually to discuss some subject in the field of neurology or psychiatry, and the proceedings are published in book form annually. At the twenty-third meeting, held in 1943, the subject of discussion was pain.

Thirty-two chapters, each consisting of an address given at the meeting, make up the contents of this volume; each is by an investigator writing on some phase of pain, and most chapters include also a discussion which followed the reading of the report at the meeting.

Most of this material has been published elsewhere by the participants in the periodic literature, but its compilation here in a single volume makes it an indispensable reference book for libraries and for individuals who have a special interest in investigation of the mechanism of pain, significance of pain in diagnosis, or methods of pain relief.

It is impossible to detail the contents of these thirty-two separate reports, and it would be improper discrimination to choose only a few for special mention; therefore, let it suffice to say that it covers all phases of pain, fundamental researches, clinical manifestations, and methods of relief.

This book is well edited, and the illustrations are very well reproduced.

Technique in Trauma. By Fraser B. Gurd, M.D., C.M., and F. Douglas Ackman, M.D., C.M., The Montreal General Hospital and McGill University. Ed. 3. Pp. 68, with 3 illustrations. Philadelphia, 1944, J. B. Lippincott Company, $2.

This book consists of a group of three papers entitled: (1) A Practical Concept for the Treatment of Major and Minor Burns, (2) A Report on the Management of Burns, and (3) Planned Timing in the Treatment of Wounds and Infections by Means of Infrequent Occlusive Dressings.

Out of a confusing welter of statements and strangely organized material it seems that the lesson the book strives to convey is that burns and many wounds are well handled by infrequent changes of dressings, a practical application of familiar experimental studies. The presentation of results with the infrequent change of pressure dressings containing a paraffin sulfathiazole emulsion is not too striking and does not impress one as more favorable than other pressure methods now in vogue. Emphatic recommendation of sulfathiazole locally and discouragement of systemic use seem to run counter to the findings of Meleny and his collaborators.

Despite the criticisms which quickly came to mind on reading this volume, it is obvious that the authors are endeavoring to evaluate fairly a method of therapy not employed widely elsewhere, and one which has much to recommend it. It is a thought-provoking little volume, and one which should be familiar to the surgeon or general practitioner whether or not he chooses to follow the techniques outlined.

Penicillin in Warfare. By several authors. Supplement to British Journal of Surgery. Vol. XXXII, No. 125. Baltimore, Md., 1944, Williams & Wilkins Company, $2.50.

Remarkable advancements have been made during World War II in the management and treatment of the wounded. There is no doubt that the availability of adequate supplies of penicillin has contributed greatly to this progress. Reports concerning the achievements of

therapy with penicillin have remained scattered. This supplement presents an excellent summary of the experience of a group of capable individuals, who composed a "penicillin team" in the Mediterranean Theatre during 1943 and 1944. It should prove to be of value, not only to those engaged with the medical problems of war, but equally informative to those in civilian medical practice.

Introductory articles record "The Principles of Medical Treatment" by Flory and Jennings; "Bacteriological Methods in Connexion With Penicillin Treatment" by Garrod and Heatley; and a brief analysis of the "Application of Penicillin to War Wounds" by Jeffrey. Scott Thompson has a helpful review of "The Bacteriological Examination of Wounds Treated With Penicillin." Detailed clinical reports include the prophylactic and therapeutic value of penicillin in soft-tissue wounds and open fractures. Gas gangrene constituted not a negligible problem in Italy, and the English concluded that penicillin definitely aided surgery and antiserum in lowering the mortality rate. On the other hand, Cutler and Sandusky of the United States Army, reporting on a smaller group of cases of gas gangrene, were unable to ascribe any significant prophylactic or therapeutic benefit to penicillin. Three papers detail a survey of the results of penicillin in war wounds of the chest and in head and spinal wounds. As a part of the problem of medicine in war, results of the use of penicillin in gonorrhea and in syphilis are presented. A bibliography summarizing most of the outstanding reports on penicillin concludes the supplement.

It is apparent that in warfare the judicious and prompt use of penicillin in wounded personnel will prevent infections, control infections, and supplement other measures in the eradication of sepsis. Throughout these reports the major theme is that penicillin is but an adjuvant to sound surgical principles and meticulous operative procedures.

This supplement is enthusiastically recommended to all surgeons. The editors of the *British Journal of Surgery* are to be commended for placing this timely information before the medical profession in this country.

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Published by THE C. V. MOSBY COMPANY, 3207 Washington Blvd., St. Louis 3, U.S.A.

Great Britain Agents: Henry Kimpton, Ltd., 26 Bloomsbury Way, London, W.C.1. Entered at the Post Office at St. Louis, Mo., as Second-Class Matter.

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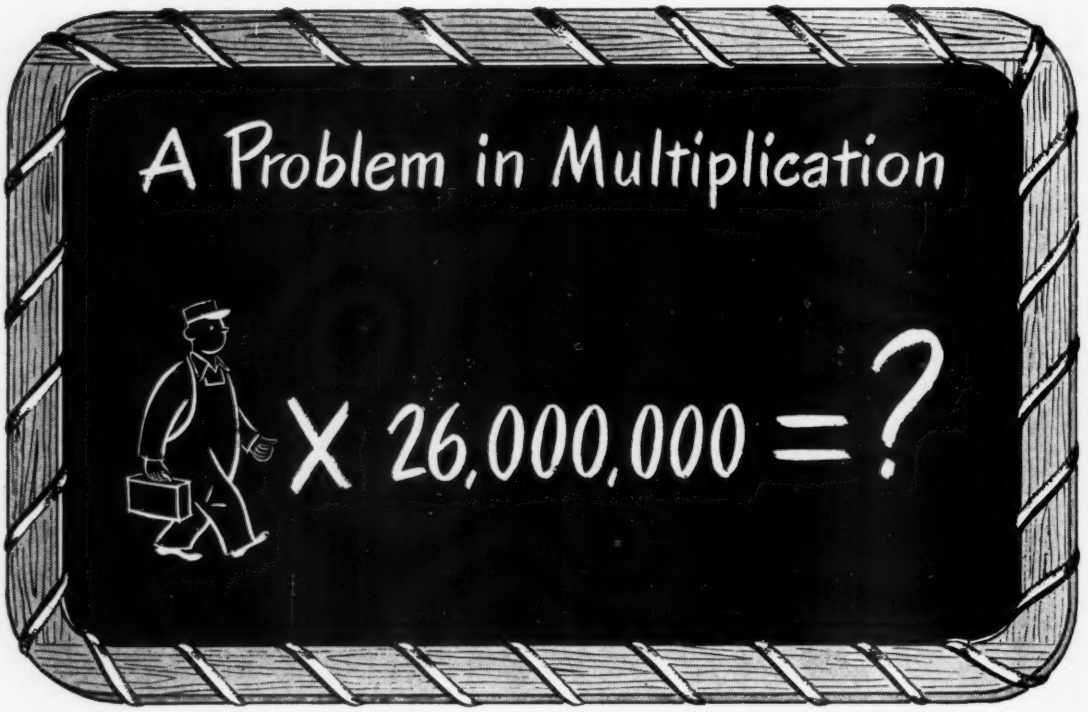

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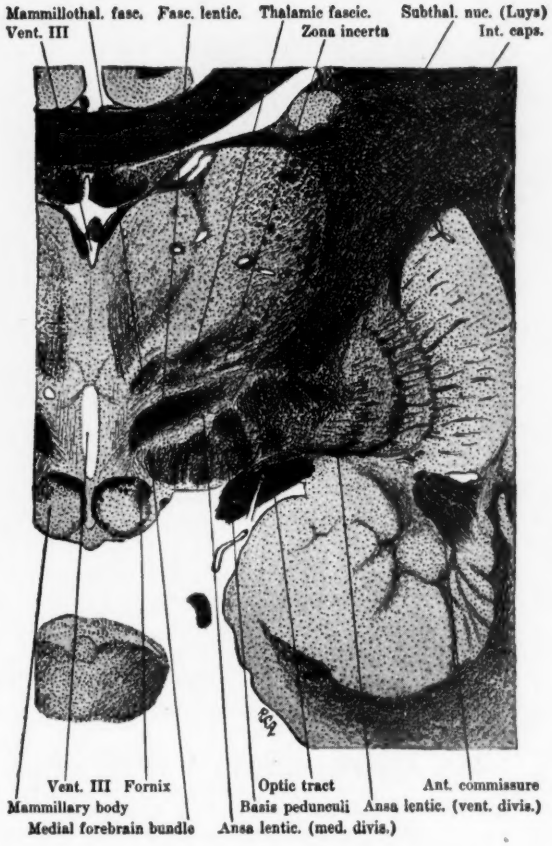

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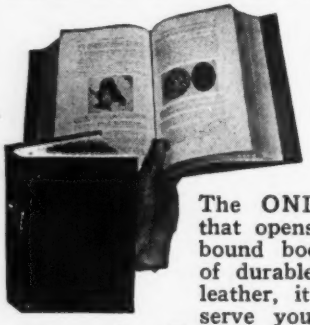

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